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Section of Comparative Medicine

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DISCUSSION ON NUTRITIONAL ANÆMIAS

The Rôle of Inorganic Elements in Nutritional Anæmia

By Sir JOHN BOYD ORR, M.D., F.R.S.

(*Rowett Research Institute, Aberdeen*)

THERE are a number of inorganic elements which have been held to play some rôle in the maintenance of the normal blood picture. The importance of iron is obvious, since it forms an essential constituent of hæmoglobin. Copper has recently been shown to affect the metabolism of iron and is therefore important. Sherman has suggested, as the result of two or three short experiments, that calcium is of importance in so far as it has a sparing effect on iron. Magnesium, arsenic, and half-a-dozen other metals have been credited with having an influence on the formation of hæmoglobin and red cells. It has not been conclusively proved, however, that deficiency of any of these elements, apart from iron and copper, can be the sole and direct cause of anæmia, though they may have an indirect effect on blood formation. Malnutrition, or defect in the metabolism arising from any cause, tends sooner or later to be associated with anæmia. It is probable that under certain conditions, the addition of some of these inorganic elements to the diet may improve the general health, and thus indirectly influence the synthesis of hæmoglobin and the formation of red cells.

Although in this paper we will limit the discussion to the rôle of iron and copper, the influence of other elements cannot be lightly dismissed. The literature dealing with them must be studied by anyone wishing to have a comprehensive view of the subject of blood formation and regeneration, and a full knowledge of the influence of the mineral content of the diet in the prevention and cure of anæmia.

Before dealing with forms of anæmia which may arise from deficiency of iron and copper, it would be well to consider briefly some aspects of the metabolism of these elements.

IRON

Metabolism.—The study of the metabolism of iron is beset with difficulties. Excretion is mainly by the intestine, hence, in balance experiments it is impossible to distinguish between unabsorbed and excreted iron, and, in histological studies, to distinguish between iron in process of being absorbed and iron being excreted. Another difficulty is that iron liberated in endogenous metabolism is partly conserved in the liver to be resynthesized.

The work of Schmidt [40] on mice, continued for several generations on a low iron diet of milk and rice to get rid of reserve stores of iron, and reduce excretion to a minimum, showed that iron is absorbed by the villi of the duodenum, and passes via the portal circulation and lymphatics to the liver and mesenteric glands.

Bunge's theory that iron can be absorbed only in organic form is no longer held. It can be absorbed only if it is soluble and ionizable. Reduced iron salts, soluble in acid solution, ferric hydroxide and adsorbed complexes of the hydroxide, ionized in acid solution [23] fulfil these conditions. On the other hand, the iron in highly complex organic compounds, which do not break down in digestion, is not available. According to Elvehjem [9], between 40 and 60% of iron in cereals is available. Most of the iron in milk is readily ionizable and therefore available [52].

Iron in foodstuffs is present largely as ferric iron, and its availability depends on the presence of acid in the stomach to convert it to a soluble form, which is then capable of reduction to the ferrous state. The absence of hydrochloric acid, therefore, from the gastric juice, which occurs in certain pathological conditions in human beings, is a factor of importance in the absorption of iron. It has been shown, however, that organic acids which may arise in fermentation processes in the achlorhydric stomach, render some of the iron soluble [2] so that even in achlorhydric subjects some reduction from the ferric to the ferrous state may take place. It is obvious in any case, from clinical results, that the reduced ferrous salt is of more value as a source of iron than ferric salts. Fullerton [15] has shown that the percentage utilization of ferrous preparations is from 15 to 20, compared with only 2·5 in the case of iron and ammonium citrate.

Requirements.—The amount of iron required by different species of animals has not been determined with any degree of accuracy. Short-period balance experiments are of little value, on account of the difficulty of assessing storage or depletion. Lintzel [27], in balance experiments on man, found that equilibrium could be established at levels varying from 2·7 to 60 mgm. per day. Stockman [47, 48, 49, 50] was able to establish equilibrium at 6 mgm. per day, and regarded that as the minimum.

A practical method of estimating requirements is to find the lowest level in diets and rations on which a normal blood picture is maintained. Stockman found an intake of 6 to 11 mgm. in healthy adults. In our investigations in Aberdeen [7] we found intakes ranging from 5·3 to 23·2 mgm. and a normal blood picture in men, but not always in women, on as low as 6 mgm. per day. These observations suggest a lower standard than the 15 mgm. per day which Sherman [43] proposed as the result of a study of 102 city dietaries in New York. In view of the difference in percentage availability of iron in different forms or compounds in foodstuffs, it is impossible to fix a limit which would be applicable to all kinds of diets. A safe level would probably be something considerably above 6 mgm. and as will be seen later, a considerably higher level is required for women of the child-bearing age.

Figures have been given for the amount of iron required for the prevention of anæmia in suckling animals, e.g. 25 mgm. in the case of pigs (Hamilton [4, 17]), but we have very little reliable information on the requirements of any of the species to prevent anæmia in later life under favourable conditions.

The iron contents of all the common foodstuffs have been worked out and are easily accessible [11, 37, 42, 46, 56]. Leafy vegetables are richer than legumes, spinach, watercress and parsley being very rich. Whole cereals are richer than milled cereals. Except in the case of infants and women of the child-bearing age, shortage of iron in the diet is probably not very common now under ordinary conditions. In our survey in Aberdeen we found no diets containing less than 5·3 mgm., the range being 5·3 to 23·2 mgm. In 102 city dietaries in U.S.A. only 5% had less than 10 mgm. (Sherman and Gillett [43]). In 47 rural dietaries the range was 9 to 32 mgm. (McKay [32]). Stockman, about forty years ago, when chlorosis was common in girls, found diets with as low as 1·2 mgm.

The iron content of milk is of special importance because it may form the sole diet for a considerable period. At the Rowett Institute in 220 samples of cow's milk a range of 0·027 to 0·140 mgm. per 100 c.c. was found. In human milk a

range of 0·15 to 0·19 was found, and Telfer [51] found in 36 samples a range of 0·05 to 0·13. There is a tendency for the iron content of milk to fall during lactation. Human milk is thus on the whole richer in iron than cow's milk. The administration of iron to the mother does not necessarily increase the iron content of the milk.

Copper

Metabolism.—The importance of copper as a factor in the formation of hæmoglobin has been established by Hart, Steenbock and their co-workers [10, 12, 19, 21, 41, 54, 55]. Rats weaned on to a diet of cow's milk developed anæmia. The addition of purified iron salts to the milk increases the store of iron in the liver, but the anæmia persists. If, however, copper be added, there is a marked reticulocyte response with a rapid increase in hæmoglobin and disappearance of the anæmia. Cunningham [5], at Aberdeen, showed that, after the administration of copper, the total amount of iron in the liver is reduced and the iron in the blood increased. Similar results were obtained by Josephs [26]. It looks as if copper were necessary for mobilization of the iron for the subsequent synthesis of hæmoglobin. Some workers [3] claim that iron alone cures milk anæmia in rats. It is probable that their results may have been due to traces of copper in the iron salts used. The balance of evidence is strongly in favour of the view that copper is essential for the synthesis of hæmoglobin.

Requirements.—In typical milk anæmia in rats 0·005 mgm. per day is the lowest amount which effects a cure. Daniels and Wright [6] in balance experiments with children, 5 years of age, found a retention of 0·034 mgm. per kg. at an ingestion level of 0·093 mgm. They suggested that 0·1 mgm. per kg. per day is required for normal children.

In a dietary survey of the poorer classes in Aberdeen, the lowest intakes were between 1·5 and 2·5 mgm. per day. In the non-anæmic families the average intake was 2·88 mgm. The amount required for adults is obviously not in excess of this level.

Milk is poor in copper. Cow's milk contains 0·012 to 0·02 mgm. per 100 c.c. (Elvehjem *et al.* [13]), and human milk from 0·04 to 0·08 (Hess *et al.* [22, 24, 58]).

In many species, though probably not in all, the young appear to be born with a store of copper in the liver. McHargue [31] showed that calf liver is much richer in copper than ox liver. Cunningham confirmed this for human liver, and for that of pigs, guinea-pigs, rabbits and rats.

It is probable that on a diet of milk only, infants may suffer from copper deficiency. Josephs found that in the treatment of anæmia of infants, there was a more rapid response when iron was supplemented by copper, and that some individuals failed to make a complete recovery on iron until it was supplemented with copper. It is probable, therefore, that in infants there may be anæmia due to deficiency of copper. Indeed, Hawksley [23] estimates that one in every twenty cases suffers from copper deficiency.

Anæmia in Animals

About ten years ago McGowan and Crichton [29] investigated anæmia in sucking pigs. The piglets did well until they were about three to four weeks old, when they began to develop symptoms of severe anæmia. In some cases the hæmoglobin fell as low as 15 to 20% of the normal. Administration of iron led to a rapid recovery, hæmoglobin rising to the normal level in about three weeks. The subsequent work of Radeff in Germany [38], and Hart and others at Wisconsin [20], showed that this was a physiological anæmia. The hæmoglobin level in the young pig falls steadily from about 11 g. at birth to about 8 g. on the tenth day. This is followed by a rise again to normal if iron be administered. If the diet be not supplemented

with iron, the fall may continue and the hæmoglobin may reach about one-fifth of the normal, which corresponds with the low levels noted by McGowan and Crichton.

There is some evidence that this physiological anæmia occurs in lambs if they are kept in confinement and weaned on to cow's milk. It has not been noted in other animals, probably because under ordinary conditions so soon as they are able to eat, adequate supplies of iron are available. It is only in the case of pigs kept in confinement on cement floors that this anæmia is common.

Under ordinary conditions anæmia due to deficiency of iron or copper has not been noted in poultry. Hart and others [18], however, have shown that it can be induced in chickens by restricting their diet to milk and maize and keeping them from getting access to soil. The condition is cured by iron. Indeed, spontaneous recovery takes place as the rate of growth slows down with the consequent reduction in the requirement for iron.

These same workers also found that, on a very low copper intake, anæmia can be produced in fowls, showing that, as in the case of the mammal, copper is essential for hæmoglobin synthesis in birds [8].

These cases of anæmia in the pig, the lamb, and chicken appear to be straightforward instances of iron deficiency in the early stages of life, following the breakdown of fœtal hæmoglobin, with the formation of hæmoglobin adapted for lung breathing, and with a demand for relatively large amounts of iron for new blood-formation to meet the requirements of the very rapid rate of growth at this stage. In older animals under ordinary farm conditions, there is no evidence that anæmia due to a primary deficiency of iron or copper is likely to occur.

Another form of anæmia which has attracted a good deal of attention in different parts of the world occurs in herbivora grazing on certain well-defined areas. This is most severe in young animals, but may occur also in full-grown animals. Nearly forty years ago, Aston in New Zealand described a condition known as "bush sickness" [1]. It occurs in cattle and sheep grazing on pumice soil and is characterized by emaciation and a progressive anæmia. Grown cattle can remain healthy in these areas for about a year; grown sheep for six to nine months. The younger the animal, the shorter the period it can be kept on these pastures without developing the disease.

Aston found that the iron content of the pasture was low and that the available iron in the soil, i.e. the iron which is extractable with 1% citric acid, is lower than in ordinary soils. He concluded that he was dealing with a simple iron deficiency. He fed iron salts and got a complete cure.

In Kenya a disease known as "nakuruitis" appears to be the same as that described by Aston [34, 35]. It also can be cured or prevented by giving the animals access to a mixture of iron oxide and common salt. A similar condition occurs in sheep in the south of Scotland [30]. It also is cured by the administration of iron. Recently a condition resembling "bush sickness" was studied in the Island of Tiree [16]. Here again the administration of an iron and salt mixture effected a cure.

Although iron salts cure this condition, it has not been established that simple deficiency of iron is the primary and only cause. In the experiments in Kenya we have found that, even after the clinical symptoms were well marked, the hæmoglobin in many cases remained almost normal—82·5% on an average, compared with 88·5% in the case of control animals showing no symptoms, and in the experiments in Tiree, the clinical signs of disease appeared before there was any definite fall in hæmoglobin. It looks as if the anæmia may be secondary to some other pathological condition, even though iron is so effective in preventing the onset of clinical symptoms.

Some recent work of Rigg of the Cawthron Institute, New Zealand [39], and Underwood and Filmer in Northern Australia [14, 53] suggests that this condition

is not due to simple iron deficiency. Underwood and Filmer found that in lambs suffering from this condition the store of iron in the liver is very high, and they claim that they can cure the deficiency by administering a residual fraction of limonite (the crude iron which Aston used) after the iron has been removed. Further work is in progress to ascertain whether copper, zinc or any of the other metals found in traces can effect a cure, and work is also planned to ascertain in greater detail the nature of the anæmia. So far, the work has been mainly from an economic point of view, to find a cure for the condition. Now that this has been done, the ætiology can be worked out at leisure.

It has been suggested that a deficiency of copper may be involved in these anæmias in herbivora which all have a general resemblance to "bush sickness" as described by Aston. In Holland "lecksucht" occurs on certain poor soils. An analysis of the pasture has shown that the copper content is only 2 to 3 mgm. per kg. dry matter, as compared with 7·5 mgm. in ordinary pastures and 20 to 30 mgm. in pastures which have a high curative value. The administration of copper sulphate with or without iron is said to effect a cure [44, 45].

In Florida a condition known as "salt sick" which affects all animals has been noted. The iron content of the pasture is said to be low [33], but iron alone does not effect a cure, which, however, is brought about by iron plus copper. It has been suggested that this condition is essentially the same as "bush sickness" and that the deficiency is of copper rather than of iron. The ætiology, however, will not be cleared up until further experimental work, including hæmatological studies, has been completed.

Human Anæmia

The physiological anæmia which occurs in sucking animals finds its parallel in human individuals. After birth there is a destruction of erythrocytes, with the accumulation of iron in the liver and a continuous fall in the hæmoglobin level in the blood until it reaches 60 to 65% of the normal. From the third month onward the hæmoglobin level rises, provided the iron intake is sufficient. If, however, the diet of the infant contains no more than that found in milk it falls further and an anæmia due primarily to iron deficiency occurs. The investigations of Helen Mackay in London, about three years ago [28] showed that about 50% of infants suffer from this form of anæmia.

In puberty unless the diet is specially rich in iron there is apt to be a transient anæmia which passes off as the rate of growth slows down and bodily functions become stabilized in the adult condition.

About thirty or forty years ago, when the dietary and hygienic conditions of young women, especially of the domestic servant classes, were much worse than they are to-day, chlorosis was common. The classical investigations of Stockman have shown that this form of anæmia was due mainly to deficiency of iron. The diet of chlorotic subjects contained, in some cases, less than 3 mgm. of iron per day, which is well below the human requirement. Chlorosis has now almost completely disappeared.

The extent to which anæmia due to deficiency of iron or copper exists in the general population is of great practical interest. Werdinius [57] found that in districts in Sweden, where the diet consists chiefly of milk and cereals, anæmia is common in adults—women suffering more than men—but is less frequent in children below 13 years of age. In East Africa, Orr and Gilks [36] found that anæmia in children among cereal eaters occurred to the extent of 39% of girls and 48% of boys, but the incidence was less than a fourth of this in tribes with a high intake of meat, blood, and milk.

In the inquiry in Aberdeen (Davidson *et al.* [7]) amongst the poorer classes, it was found that primary anæmia in adult males was uncommon. Nor was it common

even amongst school children. Of 750 school children from poor families examined, only eight were found with a hæmoglobin level below 85%. In the case of women of the child-bearing age, however, there was a different picture. Of 1,000 examined, 50% showed some degree of anæmia, and of these nearly one-third were classed as "severe anæmia." The anæmia was of the hypochromic microcytic type. It responded quickly to the administration of iron, and was therefore apparently due to deficiency of iron. It is obvious that the iron requirements of women of this age are much higher than those of men, especially with rapidly succeeding pregnancies, or in cases of menorrhagia.

An investigation is at present being conducted in several centres in England. The results of this will throw further light on the extent to which anæmia occurs in different classes of the population.

Summary

In this inadequate review of anæmias due to deficiency of iron and copper, we have discussed the physiological anæmia of young animals which occurs extensively only in the case of young pigs kept indoors, and the peculiar forms of anæmia found in certain well-defined areas among herbivora. In both cases the work of the last ten or twelve years has yielded information which enables us to prevent or cure anæmia. The economic importance of this is very great. It is probable that the ætiology of the anæmia of sucklings is now fairly well understood. The ætiology of the anæmia of herbivora, however, is still obscure. It is possible that the hæmoglobin studies now being carried out in Scotland and in Australia will throw more light upon this interesting form of anæmia.

In the case of human beings the common occurrence of anæmia in infants and among women is of clinical importance. Fortunately, both can be easily prevented or cured. So far as the evidence goes, the amount of iron and copper in the ordinary diet appears on the whole to be sufficient for other classes of human beings. More information, however, will be available within the next two or three years.

A full bibliography on this subject is given in a paper "The Nutritional Anæmias of Man and Animals," by Professor Davidson and Dr. Leitch in *Nutrition Abstracts and Reviews*, 1934, iii, 901.

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Anæmias Due to a Deficiency of the Principle in Liver which is effective in the Treatment of Addisonian Pernicious Anæmia

By JANET M. VAUGHAN, D.M., M.R.C.P.

WELL-CONTROLLED observations proving the therapeutic value of liver in the treatment of Addisonian pernicious anæmia were first published in 1926. Since that date a group of anæmias has been isolated which all respond to treatment with liver or liver extract. Included in this group are (i) tropical megalocytic hyperchromic anæmia, (ii) Addisonian pernicious anæmia, (iii) pernicious anæmia of pregnancy, (iv) tropical sprue, (v) megalocytic hyperchromic anæmias associated with *Dibothriocephalus latus* infestation, lesions of the gastro-intestinal tract and diseases of the liver. These anæmias have certain morphological features in common; they are all megalocytic and hyperchromic while the bone-marrow shows hyperplasia of the more primitive red cells. Physical signs and other laboratory findings, such as the character of the gastric secretion, may be variable. Since these anæmias all respond to treatment with liver or liver extracts they are presumably due to a deficiency of some hæmopoietic factor in liver which for brevity may be called the P.A. factor. Some members of the group respond as satisfactorily to preparations of whole stomach or autolysed yeast as they do to whole liver. It is important,

therefore, to understand what the relationship of the hæmopoietic factor in liver may be to somewhat similar factors in stomach and autolysed yeast, how these factors exert their effect in the body, and by what mechanisms a deficiency is brought about in pathological conditions.

The hæmopoietic principle in liver.—The hæmopoietic principle in liver effective in Addisonian pernicious anæmia is a relatively small, predominantly basic, nitrogenous compound, which is thermostabile and readily extracted by alcohol (Cohn, McMeekin and Minot, 1930). It is elaborated in the body by the interaction of some substance present in beef muscle and in autolysed yeast—the extrinsic factor, with a substance secreted by the stomach—the intrinsic factor (Castle, 1929; Strauss and Castle, 1932). This product of gastric digestion is presumably absorbed at some further point in the intestinal canal and finally stored in the liver (Wilkinson and Klein, 1934). It is usually assumed that the liver serves merely as a storehouse. There is evidence that the intrinsic factor secreted by the stomach is probably an enzyme (Wilkinson and Klein, 1933). Little is known of the chemical nature of the extrinsic factor. It is found in autolysed yeast, in beef-muscle, in wheat-germ and in egg-yolk. Its presence in unautolysed yeast is still open to question (Wills, 1933; Ungley and James, 1934; Lassen and Lassen, 1934). It is probably not vitamin B_1, B_2, or B_4, as has been suggested. It would appear to be some product of protein breakdown, since it occurs in substances rich in protein, and autolysis of any substance in which it is present enhances the potency of that substance (Wills, 1933; Wills and Naish, 1933; Ungley and James, 1934).

Hæmopoietic factor in whole stomach.—A hæmopoietic factor effective in megalocytic hyperchromic anæmias has been demonstrated in the dried stomach of hogs (Sturgis and Isaacs, 1929; Wilkinson, 1930) and of foxes (Wilkinson, 1933). There is indirect evidence that a similar factor is present in the stomach of some, but not all, guinea-pigs (Jacobson, 1934). It is not found in the stomachs of dogs, cows, and sheep (Wilkinson, 1933). Hæmopoietin, as the stomach factor has been called (Wilkinson and Klein, 1933), is presumably not identical with the P.A. principle in liver since the chemical properties of the two factors appear to differ. It is impossible to extract the effective principle from stomach by methods that are practical in the case of liver. Stomach extracts given by parenteral injection are inactive while liver extracts given in this way are extremely effective. Autolysis, which enhances the activity of liver, destroys that of stomach (Wilkinson and Klein, 1933). The stomach principle is thermolabile, while the effective principle in liver is thermostabile. Wilkinson and Klein (1933) have suggested, as the result of well-controlled observations on the effect of incubation of hæmopoietin with beef-muscle, that hæmopoietin is of the nature of an enzyme, probably Castle's intrinsic factor, which acts upon an unknown constituent of beef-muscle, gastric muscle, or autolysed yeast, sources of Castle's extrinsic factor, to form the P.A. factor, which is then stored in the liver. Hog's stomach is effective in treatment because dried stomach contains both the extrinsic factor in the muscle and the enzyme in the mucosa, while possibly the P.A. factor also is formed during preparation.

Addisin.—The claim that concentrated gastric juice contains yet another hæmopoietic factor which has been called "addisin" (Morris *et al.*, 1933) is probably open to other interpretation. Careful observations suggest that though a hæmopoietically active substance may be demonstrated in gastric juice concentrated by vacuum distillation, it is only found after some definite change in the gastric juice has taken place (Fouts, Helmer and Zerfas, 1934). The hæmopoietic substance is formed presumably by the action of intrinsic factor upon some extrinsic factor. In the observations in question extrinsic factor was probably provided by desquamated gastric cells and partially digested food, or may have arisen from protein substances known to be present in gastric juice (Fouts, Helmer and Zerfas, 1934).

Hæmopoietic factor in autolysed yeast.—Autolysed yeast in the form of marmite is effective in certain megalocytic hyperchromic anæmias only. It is as powerful a therapeutic agent as liver in certain cases of megalocytic hyperchromic anæmia associated with idiopathic steatorrhœa (Vaughan and Hunter, 1932), and in tropical megalocytic anæmia (Wills, 1931). It may exert some effect in rare cases of Addisonian pernicious anæmia and in megalocytic hyperchromic anæmias following gastric operations, but this is not usually maximal and may be completely absent. Extracts of marmite given by parenteral injection are without effect, even in those cases, in which, when given by mouth, they cause a reticulocyte response (Ungley and James, 1934). These observations suggest that marmite is a rich source of extrinsic factor and is only an effective therapeutic agent when the stomach still retains power to secrete some intrinsic factor.

Mode of action.—Nothing is known of the actual way in which the P.A. principle exerts its action. It is effective in extremely small quantities and can apparently be stored in the body, since it is possible to initiate a complete remission by giving by intramuscular injection 10 c.c. of a potent extract prepared from 100 grams of liver and to maintain a satisfactory red-cell count in the neighbourhood of 4,500,000 by an average maintenance dose of 2 c.c. of extract once a week. A larger dose may be given at longer intervals if preferred.

Though the mode of action of the P.A. factor is unknown, the character of the therapeutic response is consistent. A deficiency of the P.A. principle leads to an arrest of red-cell development at or near the level of the hæmocytoblast. There is extensive hyperplasia of the marrow throughout the skeleton but the hæmocytoblasts are unable to develop and pass into the blood-stream as mature red cells. When the P.A. principle is given there is immediate development of the hæmocytoblasts evidenced by the outpouring into the peripheral blood-stream of immature red cells of all types. The degree of response is most conveniently estimated by counting the number of reticulocytes. The number that reach the peripheral stream is directly related to the number of red-cells at the beginning of treatment. When the P.A. principle is given by intramuscular injection the peak of the rise will be higher than when it is given by mouth but the total number of reticulocytes put out in response to both types of treatment is the same. This effect of the P.A. principle upon the maturation of the hæmocytoblasts is entirely specific. In idiopathic hypochromic anæmia there is maturation arrest at the level of the normoblast and the P.A. principle is without effect.

Causes of deficiency of the P.A. factor.—A deficiency of the P.A. factor may theoretically be brought about in four different ways: (i) Deficient intake of extrinsic factor; (ii) deficient secretion of intrinsic factor; (iii) faulty absorption or utilization of P.A. factor; (iv) faulty storage of P.A. factor.

A deficient intake of extrinsic factor may possibly play a small part in the ætiology of many megalocytic hyperchromic anæmias. It is probably the essential ætiological factor in tropical megalocytic hyperchromic anæmia. This type of anæmia is common in Indian natives whose diet is often extremely deficient, but rare in Europeans. It is invariably cured by marmite, i.e. an autolysed yeast product, which, as already discussed, appears to be a rich source of extrinsic factor. There is deficient secretion of intrinsic factor in Addisonian pernicious anæmia. This was shown originally by Castle and his colleagues, who found that beef-muscle pre-digested with gastric juice from patients suffering from this disease failed to induce a remission, while beef-muscle pre-digested with healthy gastric juice was effective (Castle, 1929; Castle, Townsend and Heath, 1930). A few patients may possibly still retain the power to secrete small quantities of intrinsic factor, as evidenced by some response to large doses of marmite (Ungley, 1933; Ungley and James, 1934). Faulty absorption of the P.A. factor is usually assumed to explain certain cases in which liver given by mouth is ineffective while liver given by

intramuscular injection is satisfactory. In some such cases the presence of intrinsic factor in the gastric juice has been demonstrated. Many examples of sprue, some of megalocytic hyperchromic anæmia associated with organic lesions of the intestinal canal and probably all cases of idiopathic steatorrhœa fall into this group. It is possible, however, that utilization, rather than absorption, may later prove to be at fault (Vaughan, 1934). More recently, attention has been drawn to a group of cases in which megalocytic hyperchromic anæmia has been associated with diseases of the liver. It is possible that some have a true Addisonian pernicious anæmia accidently associated with cirrhosis, but in some instances the picture is not typical of Addisonian anæmia and it would appear reasonable to suppose that there is defective storage in the damaged liver (Wintrobe and Shumacher, 1933). In some such cases intrinsic factor has actually been demonstrated in the gastric juice (Wintrobe and Shumacher, 1933). In others the cirrhotic liver has been shown to contain no P.A. principle (Goldhamer, Isaacs and Sturgis, 1934). Unfortunately in no instance has the complete experiment yet been performed, i.e. the presence of intrinsic factor in the stomach been demonstrated during life and the absence of the P.A. factor from the liver after death.

Dual deficiency.—It is important, from a practical point of view, to remember that, though the essential deficiency in the megalocytic hyperchromic anæmias is that of the P.A. factor, there may also be an associated mineral deficiency. Following certain observations of Murphy (1933) I have recently given all my cases of Addisonian pernicious anæmia on maintenance treatment 90 grains of iron and ammonia citrate daily in addition to liver extract. The clinical results have been striking; without exception the patients feel better and ask to continue the large doses of iron. In some cases this clinical improvement has also been associated with a slight but definite rise in total red-cell counts and hæmoglobin. Thus patients whose red-cell counts I had never been able to raise above 4,500,000 now have counts consistently over 5,000,000 per c.mm. In the case of megalocytic hyperchromic anæmias associated with intestinal lesions it is even more important to remember the possibility of a dual deficiency. Recent work on the treatment of idiopathic hypochromic anæmia by bile salts in addition to suboptimal doses of iron suggests that in mineral deficiency anæmias also lack of the metal may not be the only deficiency present (Patek and Minot, 1934). It is essential in treating deficiency diseases in man, especially the anæmias, to remember that an adequate diet must be given as well as specific therapy.

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Dr. S. J. Hartfall (Leeds) said he had discovered hypochromic anæmia of various grades of severity among nearly one-third of 100 cases previously subjected to gastrectomy for gastric ulcer or cancer. These and other cases of anæmia following gastro-enterostomy had been studied. In 33 the hæmoglobin found was between 18 and 70%. In the remaining seven the anæmia was slight. The degree of hæmoglobin deficiency appeared to be independent of the original condition (ulcer or cancer) and of the nature of the operation performed (partial gastrectomy or gastro-enterostomy) and not directly related to the amount of stomach tissue excised. It was present in females three times more often than in males. It was essentially non-hæmorrhagic; only in four cases had traces of blood been found by the occult blood test. The clinical condition corresponded with idiopathic hypochromic anæmia and among the 40 cases nearly one-third had glossitis, half, perlèche, quarter, nail-dystrophy (one koilonychia). Splenomegaly was present in the seven most severely anæmic cases. Fragility was normal. The important differences were the superadded gastro-intestinal symptoms of which the patients complained following their operations. Thus 75% had either constant or severe attacks of abdominal pain, 60% vomiting attacks with pain, 80% flatulence and distension and 60% attacks of diarrhœa. With the gruel test-meal all the cases showed excess bile with apparent achlorhydria but when the test was repeated in 24 cases, using histamine, nine secreted free acid. X-ray observations revealed a remarkable degree of rapid gastric exit and intestinal transit. Frequently the bulk of the meal would reach the lower ileum and cæcum in less than half an hour. This was of importance in the ætiology of the anæmia for the whole upper intestinal absorption area, where iron was absorbed, was thrown out of action. One further point was of importance: owing to their gastro-intestinal symptoms the patients were led to adopt extraordinary diets which were frequently hopelessly inadequate in mineral and other hæmatinic principles. Thus, to further embarrass grossly disturbed gastro-intestinal function, the dietary intake was found to be extremely poor. The combination of these factors was, he thought, sufficient to explain the hypochromic anæmia, fundamentally an iron-deficiency anæmia, in these cases.

Dr. Price-Jones asked (1) what hæmatological standards were used in the diagnosis of anæmias in animals, (2) what were the health limits for red-cell counts and hæmoglobin percentage, and (3) whether the sizes of the red cells were considered in determining the different types of anæmia.

Dr. F. Parkes Weber wondered whether absence of the intrinsic principle of Castle was invariably associated with absence of hydrochloric acid and pepsin from the gastric secretion.[1] Was this intrinsic principle increased in cases of (apparently primary) polycythæmia rubra? He had met with temporary achlorhydria in a typical case of erythræmia—splenomegalic polycythæmia or the Vaquez-Osler syndrome.

Dr. S. C. Dyke said that the tissues in the remission stage of pernicious anæmia showed so much iron that it was difficult to believe that there could be any benefit in giving more; at three post-mortem examinations of pernicious anæmia subjects, whose blood had been restored to normal by liver treatment and who had died from other causes, he had found that the tissues failed to give the macroscopical chemical tests for iron. He agreed that iron had a place in the treatment of pernicious anæmia but not in the early stages. The indication for iron was a fall in the colour-index which might occur after even a few weeks of liver treatment.

[1] Since this meeting Dr. Weber has met with a patient (a woman, aged 38) with the characteristic hyperchromic, macrocytic blood-picture of pernicious anæmia, but without any deficiency of free hydrochloric acid in the gastric secretion [F. P. W.].

If he had understood Dr. Janet Vaughan rightly, she had said that there was evidence to show that the deficiency of the P.A. factor in the disease might be only partial. If this were so, he wondered why half-way or transitional cases were never seen, since patients suffering from pernicious anæmia either had the disease or did not have it. Nevertheless, the great differences found in maintenance dose of liver gave some support to the view that the deficiency might be partial. He had found that the maintenance dose might range from 2 c.c. of a parenteral preparation every six weeks to double that amount twice weekly.

Sir John Boyd Orr (in reply to Dr. Price-Jones) stated that in most practical studies so far, only hæmoglobin estimations had been made ; the immediate aim was to find a cure. Further studies on the type of anæmia were required. Few data existed on the normal variation in red-cell count or hæmoglobin percentage in domestic animals. Carr Fraser, working at the Rowett Institute, had made an extensive study on sheep, and had found that the variation in healthy sheep was unexpectedly wide.

Section of Obstetrics and Gynæcology

President—EARDLEY HOLLAND, F.R.C.S.

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Contraction Ring: Treatment by Amyl Nitrite, with Observations on the Pharmacological Action of Nitrite

By C. R. CROFT, D.M., M.R.C.P.

INTRODUCTION.—Contraction ring is a rare condition, but anyone who meets and recognizes it appreciates at once its reality, as well as its gravity. Surgery offers a convenient, if rather elaborate way out in this, as in other, obstetrical difficulties, but it is a ruse that offers little satisfaction as a solution to these problems, quite apart from its danger in cases where other manipulations have already taken place.

In 1927 I had the misfortune to deliver a woman with contraction ring of a fœtus affected with gas gangrene. The method adopted was morcellement, a crude and haphazard proceeding, with little or no literature attached to it. The main difficulty lies in getting the fœtal pelvis past the obstruction, which in this instance was a contracted zone from two to three inches long, and of a size closely to fit the wrist. Chancing upon a method of doing this, I feel it is worth putting it on record for future performers.

The head and arms must first be removed, and the spine cleared of ribs and abdominal walls. These are best stripped off with strong forceps, assisted by the fingers; a proceeding which is greatly helped if the cervical spine is held firmly and some traction exerted, so that as each part is removed further parts are drawn into reach of the fingers. The breech then lies above the obstruction, attached to the denuded spine. The spine is steadied by an assistant while the operator, using cleidotomy scissors, snips through the bone, close to the junction of the spine and pelvis on each side, in the region of the sacro-iliac joint. If the spine is then twisted, it is easy to divide the soft parts with a finger, and the spine is detached and removed, together with the sacrum. The symphysis pubis is then divided anteriorly, and after the soft tissues are torn through, each leg is removed separately, together with the corresponding ilium, ischium and pubis.

It is not suggested that this is a delicate procedure, but it is a possible one.

It was from a study of the literature of contraction ring, subsequent upon this that the use of amyl nitrite appeared to offer a sound and effective method of treatment, the value of which has long lain dormant and unconnected in the archives of medicine.

I propose also to describe some simple experiments on the action of nitrites on smooth muscle, which I hope will give further confidence to those who decide to employ amyl nitrite in cases of contraction ring.

History.—The history has been summarized in another paper [1] from the time of Smellie onwards. The first landmark is the thesis of Chéron, 1899 [2] in which

are described fifty-nine cases. No distinction is drawn between hour-glass contraction and retraction of obstructed labour. Where treatment is concerned, the paper is largely devoted to the comparative difficulty and danger of embryotomy and version.

In 1913 Clifford White [3] distinguished between contraction ring and retraction. In reviewing treatment he first makes the valuable observation that expectant measures are useless. He mentions the drugs in common use at the present time, chloroform and morphia, and in a list of other drugs that have been employed, mentions two cases successfully treated with amyl nitrite. None of these drugs does he regard as of material value.

In his collection of ninety cases he finds that when laparotomy was performed the maternal mortality was 31·5% and the fœtal mortality 42%, whereas in cases in which no laparotomy took place the maternal mortality was 58% and the fœtal mortality 63%.

Mr. Gilliatt [4] has recently reviewed the situation. In his total series of fourteen cases he has the satisfaction of twelve surviving mothers. In ten cases in which Cæsarean section was performed he lost one mother and no children. He mentions a case (No. 14) in which nitrite was used. His valuable comments will be mentioned later.

The six published cases of successful treatment by amyl nitrite may be summarized as follows:—

(1) Barnes' case [5].

In 1882, fifteen years after Brunton's first experiment with cases of angina pectoris, Barnes was called to a woman aged 22, recently delivered of her second child. The placenta had been retained for six hours. The external os and cavity of the cervix were fully dilated and a contraction was present at the internal os and above it, which only allowed the admission of one finger. The midwife had given ergot as soon as the child was born, and as an antidote to this, Barnes administered three drops of amyl nitrite on a handkerchief. He described the effect as follows: "During the inhalation the ring of muscular fibres round the os internum, which had been so rigid as to be absolutely undilatable, steadily yielded until I could pass the whole hand into the uterus and reach the placenta, which was universally adherent."

(2) Steele's case [6]. In the next year Steele described a similar case in which he employed amyl nitrite, having read Barnes' report.

The woman was a negress who had been delivered five hours previously and had lost a considerable amount of blood. The report continues as follows: "No effort had been made to remove the after-birth; she had been, and was still, having 'pains.' Having learned this I supposed I would have but little trouble, so I gave a dose of ergot as a precaution against after-hæmorrhage and proceeded by expression and slight traction to remove the placenta. After considerable effort and further examination I concluded that I had hour-glass contraction to deal with sure enough, and fearing that the ergot might possibly make matters worse I proceeded to make her inhale the vapour of amyl freely. When she began to feel the effects of it I handed the handkerchief to the 'granny,' that the amyl might be continued, while I made an effort to remove the placenta. The finger, as before, could easily follow the cord up to the tightly contracted part of the womb, but it would go no further and my efforts at removal failed again. All this time (only a few minutes however) she had been inhaling the amyl. I now oiled my hand and arm, determined to proceed in the orthodox way, but on introducing my hand into the vagina I was gratified to feel the placenta already slipping out of the womb. It was removed without further trouble and the woman did well."

(3) Souttar's first case [7].

The patient had been twenty-four hours in labour, with a shoulder presentation, the uterus was in a state of continuous or tonic contraction and attempts at version were futile, the ring of contraction admitting only three fingers. Embryotomy was attempted; the arms were cut off, but further progress was impossible.

The description continues: "At this juncture it happened, fortunately for the patient, that her general condition caused Dr. Kennedy to point out that she had had as much chloroform as he considered safe, if not a little more. As her pupils were rather dilated and her breathing shallow, he suggested giving a ten-minim inhalation of amyl nitrite as an antidote to the chloroform. I cannot take any credit for anticipating that which happened next; but fortunately I still had my hand in the vagina, trying to overcome the grasp of the womb and bring down a leg. My confrère snapped two five-minim capsules of amyl nitrite and held them under the patient's nose. After what seemed like an interval of about ten seconds, and suddenly, as if something solid had given way, the contraction of the womb relaxed under my hand, which passed easily up to the fundus and seized a leg, after which delivery was finished in a few minutes." No notable hæmorrhage occurred.

(4) Souttar's second case.

The patient was a multipara, who had been in labour for twenty-four hours and appears to have had a contraction ring. Souttar bore in mind his previous experience, but understood the value of a control. In his own words: "For the sake of accuracy we decided to make an honest try to deliver with chloroform alone if possible." Attempts with forceps failed and he was satisfied that delivery by this means was impossible. The inhalation of ten minims of amyl nitrite was followed by sudden delivery, Souttar's description being as follows: "So sudden and completely did all contractions cease from that moment that the child was lying on the bed before my colleague, having given the inhalation, had time to fetch his bag from the next room." There was no post-partum hæmorrhage.

(5) The fifth case I saw myself.

A woman of 43 was in the eighth month of her eleventh pregnancy. Labour pains began at 10 a.m. and were described as terrible, until the membranes ruptured at 2 p.m. Pains then ceased until at 4 p.m. she had a severe pain, which was followed by considerable hæmorrhage. Examination at 4.30 p.m. showed the vagina and lower uterine segment to be distended with blood-clot. The os was perceptible as a slack ring in the wall of the lower uterine segment and at a distance of 1½ to 2 in. above the os, the uterine wall was contracted to form a rigid canal extending upwards for at least 2 in. and of a uniform diameter of about 2 in. Through it could be felt the lower limbs of a premature infant. A leg was brought down, a fillet attached to the ankle and firm traction made upon it. This resulted in avulsion of the foot. The other leg was brought down and the abdomen of the fœtus was now compressed by the ring so tightly that no further progress could be made. Conditions were unchanged for ten minutes, when an inhalation of six minims of amyl nitrite was given. For one minute no change could be felt in the consistency of the ring, but at the end of this time traction on the trunk caused easy descent of the fœtus and further examination was not practicable. Delivery was complete in three minutes. There was little trouble with the placenta, and hæmorrhage was slight.

(6) Gilliatt's case.—Mr. Gilliatt's comment is as follows:—

"In one of my cases, No. 14, three minims were used with magical effect, and I feel sure it is worthy of use in all cases in which the cervix is sufficiently dilated to enable delivery to be completed if relaxation of the ring can be obtained, and also in cases of hour-glass contraction during the third stage of labour. I feel doubtful of its value in cases in which cervical dilatation is small in amount, not more than two or three fingers.

The history and early uses of nitrites.—I propose to deal mainly with work which appears to have a direct bearing on the matter in hand. A more complete résumé is available [8].

The first publications of a pharmacological action of nitrite were made in 1859 by Guthrie [9], who noticed flushing of the face, throbbing of the carotids and acceleration of the heart's action in the human subject.

Unpublished experiments by Dr. Arthur Gamgee showed that amyl nitrite greatly reduced the arterial tension, in both animals and man. He observed that the sphygmographic tracing of the radial pulse underwent remarkable change, the waves becoming much more frequent, and their ascent, and—especially—their descent,

much more rapid, while the pulse-rate and the pressure in a manometer connected with the carotid of a rabbit fell when a vapour of nitrite was inhaled.

The first experiments of Gamgee were witnessed by Lauder Brunton who, while house physician at Edinburgh Infirmary, observed that bleeding, to the extent of two or three ounces, was the most effective method of relieving pain in cases of angina pectoris. He therefore decided to employ a drug which had the power of lessening blood-pressure.

In the spring of 1867 [10] he obtained some pure nitrite from Dr. Gamgee and later a less pure product from Macfarlan and Co. and with the permission of Dr. Hughes Bennett he administered the drug to a blacksmith suffering from angina pectoris, combined with aortic obstruction and regurgitation. Relief of symptoms following in from thirty to sixty seconds.

The main interest of the case, in connexion with the present inquiry, lies in the record of pulse tracings taken on May 28 before and during an attack, and also while the attack was being relieved by nitrite [11]. These support the clinical observations on the pulse, in showing that during the attack of pain there is a great lessening of the elasticity of the pulse-pressure, and that the effect of amyl nitrite is to hasten the restoration of the pulse diastole. Clinical observations showed in addition that as the pain increases in severity, the pulse becomes smaller and the arterial tension becomes greater. The pulse tracings therefore indicate not a defective systolic rise, but rather a defective relaxation of the walls of the arteries.

Brunton's comment runs as follows :—

> " This form of curve clearly indicates that the arterial tension is much increased and this increase can, I think, be due only to contraction of the small systemic vessels, so sudden and so great as well to deserve the name of spasmodic." The nitrites would appear to bring about a restoration of the " vascular diastole."

The direct action of nitrites on smooth muscle.—Little work appears to have been published to show the direct action of nitrites on smooth muscle.

Cow [12] performed twelve experiments with lengths of artery suspended in saline, to which a solution of sodium nitrite was added. Dilatation in these cases was abrupt in character, the maximum degree of dilatation was soon attained and the vessels remained dilated for a considerable time.

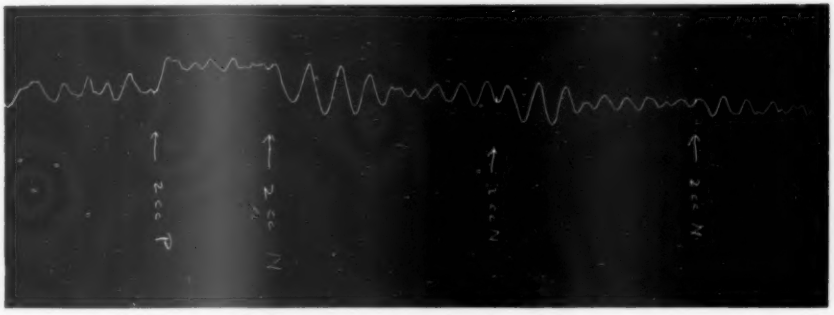
Atkinson's experiment [13] on ureters is often quoted: A rabbit was killed by bleeding, and kept in a hot chamber. Saline was passed through one ureter and saline with nitrite added to it was passed through the other. There was marked dilatation with nitrite, shown by the increase of flow of the fluid.

It will be seen that investigations into the actions of nitrites show a singular lack of simple experiments. Primary issues have been overlooked by reason of the overwhelming importance of the cardiovascular effect.

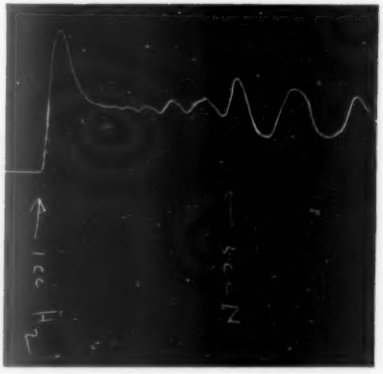
Investigations were therefore undertaken to decide the effect of nitrites on uterine and intestinal muscle under simple experimental conditions. I have to thank Professor J. A. Gunn for much help and advice in this work.

Tissue was taken from guinea-pigs, rabbits and man. Strips of tissue were suspended in a vessel containing modified tyrodes solution and kept at 37° C. by means of a water bath. A stream of oxygen was bubbled through the solution. The vessel contained about 100 c.c. of fluid, which could readily be changed. Drugs to be tested were introduced into the tyrode by means of a pipette and gently stirred, and tests were made to show that this did not vitiate the result. Changes in length of the muscle were recorded by means of a straw lever on a slowly moving kymograph. The cardinal difficulty was the experimental production of a spasm which in any way approached the intensity observed in a contraction ring.

In twenty-one trials in which a condition which could be called a spasm was produced, eight followed the use of histamine, four apparently resulted from a lack of oxygen, two followed the use of adrenalin, two, the use of pituitrin plus a lack of oxygen, one, the use of barium chloride and four were unaccountable. Histamine therefore appeared to be the most effective method of producing the necessary spasm. A lack of oxygen was found to produce some degree of spasm, but this was liable to sudden spontaneous remissions, so that nitrite effect was not always clear.



Human uterine tissue. Slight irregular contractions at raised tone following pituitrin (P). Appreciation of nitrite (N) to this is followed by great improvement of beat, affecting mainly diastole.



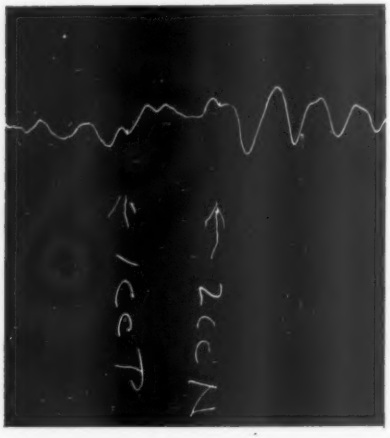
Human uterine tissue: Slight rhythmical contractions at raised tone following histamine. Greatly improved rhythmical contractions following application of nitrite.

An effective spasm can be produced by administering pituitrin and then shutting off the oxygen.

The results of seventy-six trials of the action of nitrite on smooth muscle under various circumstances can be summarized as follows:—

Commentary on experiments.—It will be seen from this (column 1, page 43) that under experimental conditions nitrites tend to have no effect upon the normal rhythmical contractions of smooth muscle. Large doses cause a gradual weakening of beat, with a final cessation of diastole.

Human uterine tissue. Increased "tone" with absence of rhythmical contractions induced by histamine. Application of nitrite is followed by restoration of rhythmical contractions at slightly lower level.



Human uterine tissue. Increased tone with slight irregular contractions following pituitrin. Application of nitrite is followed by restoration of rhythmic contractions.

In three instances a temporary complete cessation in diastole of the beat of uterine muscle of the rabbit was obtained, but a similar effect was not obtained with any other tissue. On the other hand, the more the condition of the muscle tends towards spasm, the more change does nitrite produce.

An increase in the tone of smooth muscle, with continued rhythmical contraction, can be produced with comparative ease (columns 2 and 3), but upon this nitrite has uncertain effect. If, however, a cessation of the beat in the systole can be produced (column 4), nitrite tends to cause a restoration of diastole, and in this manner the rhythmic beat is restored, the restoration being sometimes accompanied by a lessening of tone.

	Effect of Nitrite				
Type of contraction	No change	Restored or improved rhythm at the same or at a raised level	Restored or improved rhythm at a lower level	Prolonged diastole (A) or temporary relaxation of spasm (B)	Cessation in diastole
1. Normal contractions (14)	12 (or 86%) ...	— ...	1 (7%) ...	— ...	1 (7%)
2. Regular contractions at a raised level (16)	6 (37·5%) ...	1 (6%) ...	7 (44%) ...	(A) 1 (6%) ...	1 (6%)
3. Irregular contractions at a raised level (21)	6 (30%) ...	1 (5%) ..	13 (62%) ...	(A) 1 (5%)	
4. "Spasm" (21)	4 (19%) ...	3 (14%) ...	8 (38%) ...	All (B) 6 (28%)	

Unclassified 7. All showing weakening of the beat in various degrees.

Clinical evidence in support of this is provided from two sources. First, Lauder Brunton's pulse-tracings in a case of angina pectoris. Secondly, the effect of sudden delivery in cases of contraction ring of the uterus treated by nitrites, without any ensuing flaccidity of the muscle-wall, such as would give rise to post-partum hæmorrhage. An absence of post-partum hæmorrhage is one of the more striking features of the nitrite treatment of this condition.

The administration of nitrites may be regarded as a safe and efficient method of treating contraction ring.

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Discussion.—Mr. W. Gilliatt said that he had used amyl nitrite in cases of this condition, and considered that it was of the greatest value in cases in which there was sufficient cervical dilatation for delivery to be completed at once, but he was not sure that it was of value when the dilatation of the cervix was small—i.e. about two fingers. He had met with six cases this year, but in one amyl nitrite was not used. In the three cases in which it was used, it caused immediate and complete relaxation of the ring, so that delivery could be completed at once by forceps without any unusual amount of traction. In the two cases in which it failed, one patient had inhalations during two succeeding pains, an ampoule containing 5 minims of amyl nitrite being broken under the anæsthetic mask for each pain. In this case Cæsarean section was carried out subsequently. In the second case in which it failed, it was used for an hour-glass contraction during the third stage of labour. The placenta was retained, owing to this condition and rapid injection of the umbilical cord with saline failed to make delivery of the placenta possible. A hand was passed into the uterine cavity and it was

found that two fingers would not pass through the ring. An ampoule containing 3 minims of amyl nitrite was broken under the anæsthetic mask and relaxation immediately occurred, allowing four fingers to be passed, but before separation of the placenta could be carried out, the ring had re-formed and had to be dilated manually in order that the placenta might be removed.

Mr. CHASSAR MOIR: Much of our knowledge of contraction ring is due to the work of Clifford White who, many years ago, clearly distinguished between *retraction* ring (or ring of Bandl) on the one hand, and *contraction* ring on the other. Even now, the two conditions are sometimes confused; especially is this so in American literature where Bandl's ring is often wrongly called contraction ring. Mr. Clifford White has given me permission to show his excellent specimen of a uterus with a contraction ring. This specimen has already been shown to the Section, and is fully described in the *Proceedings*, 1913, vi (Sect. Obst., 70), but no apology is needed for showing it once more. The patient was in labour for five days, the membranes having ruptured on the second day. An attempt was made by the patient's doctor to perform internal version because of a prolapsed hand. On admission to hospital it was found that intra-uterine manipulation was impossible because of a tight constriction of the uterine wall around the fœtus. Morphine, gr. $\frac{1}{3}$, and deep chloroform anæsthesia did not relax the spasm. The abdomen was then opened, and a hysterectomy performed with the fœtus still *in utero*. The specimen is remarkable for the thick muscular constriction which has formed in the groove of the fœtal neck. The thickness of the uterine wall above and below the constriction is very nearly the same—a state of affairs quite different from the findings in cases of mechanical obstruction associated with retraction ring.

My own experience of contraction ring concerns one case. A patient aged 35, and pregnant for the first time, had been in labour thirty-eight hours. Her general condition was good, but as the second stage had lasted about six hours and she was beginning to show signs of distress, the forceps was applied. It was found that the fœtal head could be brought down as far as the vulva, but when the pull was relaxed the head receded into the vagina. When it was seen that no progress was being made with a reasonable amount of traction, the forceps was removed, and a hand passed into the vagina. A broad, tight band of uterine muscle was felt around the fœtal neck making it impossible to reach up to the shoulders. Forceps was reapplied; amyl nitrite was administered on the anæsthetic mask till the patient showed marked blushing, and the anæsthetic was then deepened. Traction was resumed, and the fœtus (7 lb. in weight) was delivered with ease.

Dr. Croft's experimental work on nitrites has interested me in another respect. Since nitrites relax uterine spasm so successfully, it seems reasonable to give them in cases of intrinsic dysmenorrhœa. This suggestion was made to me some months ago by Dr. Rae Gilchrist, and I have already tried it in a few cases. Unfortunately the results so far have been disappointing, but in view of the experimental work presented to us to-night, it may be worth while to give a further trial to this line of treatment.

Mr. JAMES WYATT related two cases. The first he saw in 1932; the patient was a primigravida. Twenty-seven hours after labour commenced the os was not fully dilated but forceps were applied. Five and a half hours later the os was dilated, and forceps were applied again, but the head could not be moved. A very tight contraction round the neck of the fœtus was found. Two injections of morphia, one-sixth of a grain, and a capsule of amyl nitrite had no effect. Five hours later he applied forceps, but was unable to shift the fœtus; he put his hand in, and found the ring still present. Ether was used, and a capsule of amyl nitrite was broken in the Clover's inhaler, and within two minutes there was relaxation and the fœtus was easily extracted.

In another case, also in a primigravida, there was a tight ring. Nitrite of amyl was given in a Clover's inhaler, and with gentle pressure the placenta was expelled.

Dr. CROFT (in reply to Mr. Chassar Moir) said that Leech had described the use of nitro-glycerine in tablet form, for dysmenorrhœa, and reported that it was of service.

He suggested that sodium nitrite, 1 gr., should be employed in a similar manner.

[*January* 18, 1935]

The Estimation of Fœtal Maturity by a New Method of X-ray Cephalometry : Its Bearing on Clinical Midwifery

By L. N. Reece, F.R.C.S.

Abstract.—A plea is made for routine use of X-rays in antenatal work.

A new method of cephalometry is described, depending on the fact that the fœtal head is a rough ovoid. It is shown that the shadows cast by ovoids may be oval or circular, but that always the diameter of the greatest circular section of an ovoid is represented in its shadow—by the diameter if the shadow be circular or by the short axis if oval. The results are applied to estimate the actual proportions of fœtal head and maternal pelvis, and also to estimate fœtal maturity.

The accuracy of the method of cephalometry was tested in 100 cases of labour induced by rupture of membranes.

A simple method of pelvimetry is described, and it is suggested that pelvimetry should be carried out in the early months and not later when the pelvis is obscured.

No special apparatus is required and any cottage-hospital X-ray set will serve.

For many years before the introduction of X-rays, attempts were made to estimate the size of the fœtal head relative to that of the maternal pelvis. All who have done antenatal work are aware of the limitations of the usual clinical methods. In about 10% of cases it is difficult, and in 5% impossible, to decide with certainty whether a fœtal head will pass safely through the pelvic brim. In no case is it possible to estimate fœtal maturity within three weeks by palpalpation alone. Reliance must be placed on dates which are frequently untrustworthy. The results of this uncertainty are reflected in the immature babies born after unnecessarily early inductions, in grossly over-mature babies of 12 lb. and over, in the physical and mental sufferings of patients, and in the costly, irritating waiting of nurses in cases where the dates have proved widely inaccurate.

It is suggested that antenatal work without the routine use of X-rays is no more justifiable than would be the treatment of fractures. In this country, to-day, skiagrams are taken of every trivial injury for fear of a charge of neglect. In midwifery the immense possibilities of X-rays are ignored to such an extent that the head of a large antenatal clinic was heard to boast that no such examination had been made for his clinic for years! Why is this? The answer is simple: obstetricians and radiologists have not collaborated sufficiently, and the information obtained from skiagrams has not been thought sufficiently helpful to justify the trouble and expense involved. In most clinics, it is true, skiagrams are now used in special cases to get a rough idea of the relative sizes, and in a few, exact pelvimetry is carried out, but usually no attempt is made to arrive at exact figures with regard to the fœtal head. It has been said that to obtain measurements, of any value, of the fœtal head is impossible because of the number of varying and incalculable factors. It is claimed that this is not so, and it is the object of this paper to show that it is possible for any trained nurse, radiographer, or doctor, who can recognize a fœtal head by palpation, to determine the actual diameters of the fœtal head and from these figures to estimate fœtal maturity.

If this claim proves to be justifiable, then the whole outlook on the use of skiagrams changes, for even exact pelvimetry is almost meaningless without exact cephalometry.

The work of Thoms in America and of Roberts, Rowden, and others in this country has placed X-ray pelvimetry on an exact basis but, unfortunately, most of these methods require high-powered plant and the tendency is in the direction of increasing complication in search of meticulous accuracy. This has resulted in

delay in their adoption and there has been no such general increase in the use of X-ray pelvimetry as might have been expected. Undoubtedly one or other of these exact methods will one day be in universal use, but is accuracy to one tenth of an inch of such vital importance clinically, that while waiting for thousands of pounds to be spent on plant, patients must be deprived of the help of X-rays? There is no doubt that once the clinician realizes what can be done, the general demand will bring refinements of technique quickly enough. The method of pelvimetry mentioned later will serve its purpose if its simplicity introduces users of cottage-hospital sets to this valuable work and so to other and better methods. It seems certain that in time students will be taught to recognize pelvic abnormalities clinically and then to see them in skiagrams and that cephalometry will be carried out in all cases. What justification can there be for "trial labour" when X-rays could show that failure was almost inevitable? Almost all of what is scornfully termed "meddlesome midwifery" is born of fear and uncertainty, and the courage and patience necessary to watch a labour for many hours under home conditions go only with conviction of a successful outcome or with total lack of imagination. The day is to be welcomed when obstetricians, instead of recording with pride the birth of babies exceeding 14 lb. in weight, will admit with shame that they have allowed a baby to exceed 9 lb.

The Diameters of the Fœtal Head

Theoretical considerations.—It is proposed to measure the bi-parietal diameter, for the method lends itself only to this, and fortunately this diameter is also the

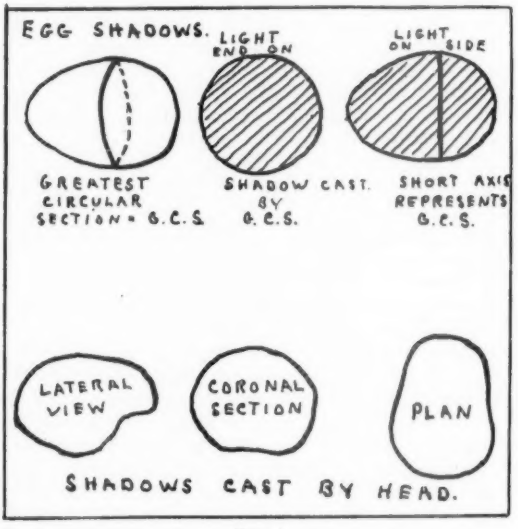


Fig. 1.

most important. For purposes of X-ray examination the fœtal head is, in the essential characteristic, an ovoid. The shadows it casts may be compared with those cast by an egg. As indicated in the diagram, a cross section through the thickest part of an egg is circular and the point to be grasped is that some diameter of this "greatest circular section" must be represented in any shadow cast by the egg (fig. 1).

The shadow may be circular or oval but if it be circular it is the shadow cast by the outline of the greatest circular section or if it be the oval then the short axis of the oval must represent some diameter of this section.

In fig. 1 is shown a model of a fœtal skull in profile, in plan, and in coronal section through the parietal eminences. The facial bones, being still in cartilage, do not show in a skiagram and the model is shown correspondingly deficient in profile.

Here is the ovoid and here may be seen the all important "greatest circular section." It is true that it is not an exact circle but, where necessary, this can be allowed for. The unquestionable fact remains that the shadow cast by the head may be circular or oval, but if it be circular it is the shadow cast by the circumference of the coronal section, and if oval then the short axis of the oval must represent some diameter of the coronal section.

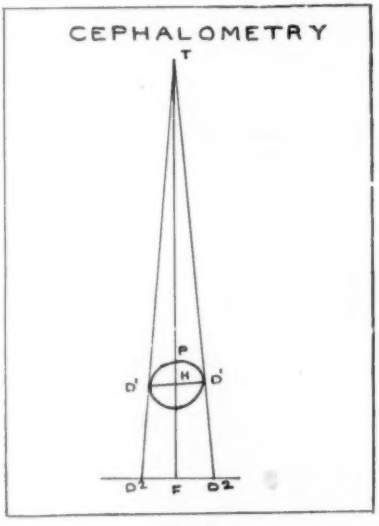


FIG. 2.

T = Tube. F = Film.
D^1 = Diameter of head. D^2 = Diameter on film.

$$D^1 = D^2 \times \frac{T\,H}{T\,F}$$

In other words the attitude of the head in the pelvis is no longer of vital importance, for every skiagram must show a diameter of this greatest circular section and it can be measured.

The mathematical problem (fig. 2).

It is clear that $\frac{T\,H}{T\,F} = \frac{D^1D^1}{D^2D^2}$

Now T F is a known constant—the tube—film distance.
D^2D^2 the film diameter can be measured.
There remains T H.

How is it possible to measure from the tube to the centre of an unknown plane somewhere in the abdomen or pelvis? It can be said at once that exact measurement is not possible, but a high degree of accuracy is not essential, for it

must be recognized that an error of 1 in. either way will affect the result by at most 0·15 in. and in practice very little error appears. The distance T P is measured from the tube to the nearest part of the head that can be palpated. The factor P H is added after consideration of the size and type of shadow. It will usually be about 2 in. but may vary from 1¼ to 3 in. The figures below show some common positions of the head and the shadows which result. They show how, apart from the size of of the head, the distance P H may vary, but they also show how the amount to be allowed can be calculated. Each type of shadow shown can be caused only by the corresponding position of the head.

If the head be near full term :—

In fig. 1. H is at the level of the parietal eminences and will be about 2 in. from the base of skull (the point palpated would be about the mastoid).

In fig. 2. H is midway between the parietal eminences and P H would be about 1¾ in.

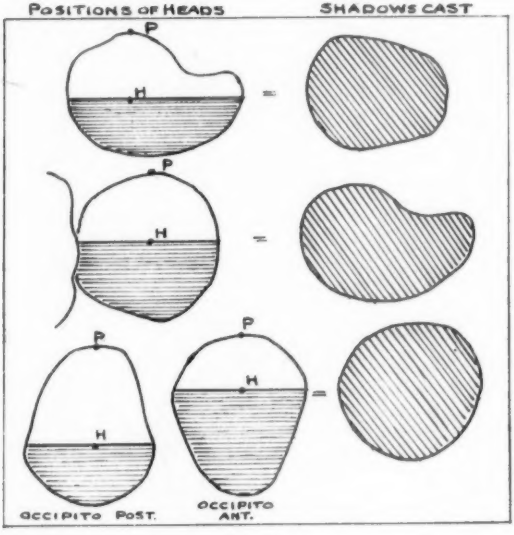


FIG. 3.

In fig. 3. In one case the sinciput and in the other the occiput is felt. P H would be about 3 in. and 2 in. respectively. Which position of the head was present can be settled clinically or by the skiagram.

In the case of all oval shadows P H may be taken as 2 in.

It will be seen, therefore, that if P H were taken as 2 in. in all cases near term very little error would result. The allowance should be reduced in proportion when the head is obviously smaller, remembering that the bi-parietal diameter at thirty-two weeks is 3 in. If a high degree of accuracy is aimed at, the size and shape of shadows should be considered, and the error in P H should be below ½ in., which in the final result represents only 0·07 in.

Practical application of the method.—The patient lies comfortably on her back on the table. The focus film distance chosen is 30 in. The plant available for this investigation would not work at a greater distance, but where a greater focal distance is possible, all errors will be reduced. The head is carefully palpated, and the level

of the highest point noted. (N.B.—The head *must* be identified; the mistake most likely to be made, and most serious, is to mistake the anterior shoulder for a head which is low in the pelvis.)

The tube is centred over the point palpated, and the measurement T P is made to this point by means of a telescopic measuring rod attached to the tube. This is easier and more accurate than using a tape. Allowance is made for the thickness of the abdominal wall. In cases of difficulty the head level may be compared with the level of the symphysis pubis, and measurement made to the latter with the appropriate adjustment.

The measurement T P is recorded and the exposure made. After development the short axis of the shadow is measured, using for convenience a ruler graduated in tenths of an inch. After consideration of the size and shape of the shadow, the factor P H is added to T P. In the first instance it may be taken as 2 in. Reference is then made to the table, and the answer is at once read off.

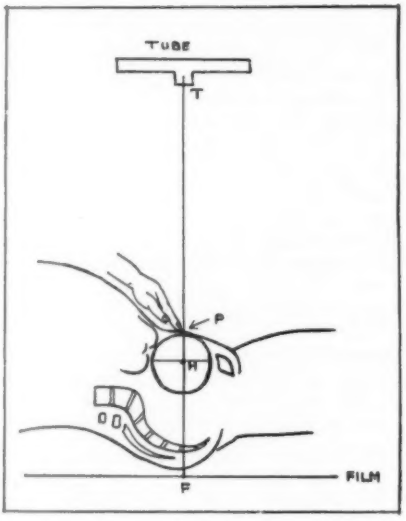


FIG. 4.

T P = Tube to head. T F = 30 inches constant.
P H = Allowance to short axis centre (usually about 2 in.).

Interpretation of the result.—If the coronal section were a true circle, the result would in all cases represent a diameter, and would need no adjustment. Unfortunately, the sub-occipito-vertical diameter is, at term, 0·25 in. less than the bi-parietal, and it becomes necessary to identify the diameter concerned in the shadow, and in some cases to make additions to bring the result up to the bi-parietal diameter. As a rule the shadows are not equivocal and the correct addition is easy to gauge:—

(1) In the plan shadow (see fig. 7, in Appendix) the short axis is clearly the full bi-parietal diameter.

(2) In the true lateral (evidenced by the lines of the orbital plates being superimposed) the short axis is clearly the sub-occipito-vertical. Here, near term, 0·25 in. must be added. As a check, the sub-occipito-bregmatic diameter may be measured, for the fontanelle is clearly seen.

(3) Long oval shadows vary between lateral and plan views, and here the gradation is usually clear. For instance, as the lateral view becomes impure the lines of the orbital plates separate and then disappear and first one and then both parietal eminences appear. Thus, near term, the addition necessary to bring the calculated diameter up to the full bi-parietal diameter will vary from 0·25 in the pure lateral view to nil in the plan view. When the head is smaller the addition will vary in proportion.

Circular and nearly circular shapes.—Here a difficulty arises in deciding what the short axis, if any, represents. If the shadow be almost exactly circular then the diameter is definitely equal to the bi-parietal. If there be a short axis it may be the sub-occipito-vertical or the bi-parietal itself. The decision as to which can be made by observing at what point the shadow of the spine joins the head shadow. This fixes the sub-occipital region.

If the long axis ends where the spine joins, then the short axis represents the bi-parietal diameter.

If the short axis ends where the spine joins, then this axis may represent:—

(*a*) The true sub-occipito-vertical. In this case the spine shadow ends sharply at the head shadow, or (*b*) some length between the sub-occipito-vertical and the bi-parietal. This is indicated by the spine shadow entering the head shadow a short distance. (This can be seen only in clear films.) It is again stressed that the short axis cannot be more than the bi-parietal or less than the sub-occipito-vertical.

The finer adjustments are a matter of practice and familiarity with the shadows but if the shadow shapes are considered at all it is almost impossible to make an error from this cause exceeding 0·15 in. After a brief study of films the shadow types will easily be recognized.

The method is equally applicable to twins and breech presentations, though a preliminary film may be necessary to identify the head with certainty.

Calculation of Fœtal Maturity.

This is the most interesting and valuable development that has arisen out of the method. It has been shown by Calkin that the diameters of the head are proportional to the length of the fœtus. Calculating from tables of age for length, it was found that

at 32	weeks	the	bi-parietal	diameter	= 3 in.
„ 36	„	„	„	„	= 3·3 in.
„ 40	„	„	„	„	= 3·75 in.

These are, of course, average figures, but comparatively few babies depart widely from the average rate of growth, and the great majority are born with a bi-parietal diameter very near 3·75 in. It will be noticed that in the table the bi-parietal diameter increases almost exactly $\frac{1}{10}$ in. each week during the last eight weeks and for purposes of calculating maturity this increase may be taken as exact. Thus, if by X-ray calculation, the bi-parietal diameter measures 3·5 in. it may be said that in two and a half weeks it will measure 3·75 in., i.e. that if the baby is to be born of average size it will have reached full term. The coincidence of the steady increase of $\frac{1}{10}$ in. each week is so convenient as to arouse scepticism, but repeatedly, in dealing with small head shadows, the date forecast in this way agreed with the period calculation and with the actual event with an exactness that was entirely unexpected.

Weight of fœtus.—It is not possible to predict the weight of a baby from these figures with any precision, because weight is not proportional to size of head—e.g. a baby may be small-boned, but very fat, or vice versa. Post-maturity commonly goes with excess of fat, and if the X-ray date and period date agree, but delivery

does not take place until appreciably later, then the head will be larger than normal and weight will be full or excessive according to the degree of post-maturity.

Accuracy of the method.—It is obvious that the value of this method of forecasting maturity depends on the accuracy of the head measurement.

It may be of interest to record that this method of X-ray cephalometry and calculation of fœtal maturity was worked out to act as a safeguard against prematurity in an investigation into induction of labour by rupture of membranes.

During the past two and a half years over 100 cases of induced—and many of spontaneous—labour, have verified the predicted measurements, with a maximum error of 0·2 in. Measurements were taken soon after labour, or later, if moulding were present. Induction was carried out in some cases three, four, or five weeks before full term as calculated by the period. In no case was the calculation seriously at fault nor, with one exception, has any baby died since birth. The exception justified the method, for owing to absence, induction was not performed until a fortnight after the date selected. Clinically it was held in this case that the head would pass the brim, and in fact it did so, but as a very tight occipito-posterior. A 7½-lb. baby was extracted with difficulty, after rotation, and survived only forty-eight hours. In this case there was no justification clinically, but every justification from the X-ray findings, for an earlier induction.

In two consecutive cases the X-ray date for full term differed from the period date by over four weeks and although the period date was supported by quickening (as remembered) and by the size of the uterus, in both cases the X-ray prediction was dramatically justified.

It was only as the investigation proceeded that the full possibilities of the method became evident, and the comfort, in practice, of the information gained has to be experienced to be believed. Many minor theoretical objections to the method may be raised, such as, for instance, the fact that tangents drawn from the ends of a diameter of a circle could never meet at a point (the tube in this case) and again that in calculating the P H factor one assumes to some extent the maturity one sets out to determine, but in both cases the error involved is negligible, and the hard fact remains that for over two and a half years it has worked in practice and, moreover, almost as well in its first rough conception as in its present more elaborate form.

At first the results were used with serious misgivings and every effort was made to obtain clinical confirmation, but they are now relied upon with confidence, to the satisfaction of all concerned.

Some clinical considerations.—The outstanding advantage of the information gained by this procedure lies in the possibility of an approach to scientific control of the time for labour. Where necessary, labour can be induced at such a time as will safeguard mother and baby. Unnecessary Cæsarean sections can be avoided. It is possible to say with certainty that a head will pass the brim or to say that there is a risk which should not be accepted. Some "trial labours" which result in a living child are entirely unjustified and should not have been risked. Many Cæsarean sections are performed with no justification except the difficulties of clinical examination. It would appear obvious that labour induced by rupture of membranes is a better risk for a primipara than a 12-lb. baby, and that a breech presentation which cannot be turned, at least should not be allowed to become post-mature. The roomiest pelvis does not justify extensive laceration of soft parts.

The combination of cephalometry with induction by rupture of membranes presents such attractions that, in the hands of the careless, inductions for convenience will result in harm, but given an intelligent consideration of the relative sizes of the fœtal head and of the maternal pelvis, nothing but good can come of it.

Fœtal maturity, as estimated by X-rays, should be considered in relation to the

date calculated from the last menstrual period, for though this is usually slightly exceeded and is sometimes a month out, yet this date represents as nearly as we can fix it the end of the full period of gestation. The principle to be acted upon is that where the period date and the X-ray date agree within say ten days, the period date should be trusted as showing the normal gestation period for that particular baby and induction should never, without good reason, be performed before that date. If, however, there be a difference of about a month, then that date which is four weeks before or after the period date (as indicated by X-rays) should be chosen as representing full gestation. In any case in which contracted pelvis is under consideration, the size indicated by X-rays should be accepted and acted upon. It is highly improbable that an error will be made which will affect the viability of the baby or the possibility of successful delivery.

The rate of growth of the head is so reliable that a decision to induce labour may be acted upon several weeks later than the X-ray date, though in borderline cases the examination may be repeated for confirmation.

The place of cephalometry in antenatal work would appear to be :—

(1) To determine whether the date of full gestation as calculated by the menstrual period be correct.

(2) If no period dates are available, to fix an approximate date for full gestation.

(3) To estimate the probable size of the baby (large or small), from the estimated bi-parietal diameter at term (useful for primiparæ and in cases of small pelvis).

(4) To help in the decision on a date for induction in cases of postmaturity or relative disproportion.

X-ray Pelvimetry.

At a time when new methods of exact pelvimetry are crowding in, there would seem to be little justification for mentioning one which does not claim to be exact. The question of simple pelvimetry is raised here as part of the plea for universal use of X-rays in antenatal work. In the cases which were the basis of this work so much help was obtained from this elementary method that it more than justified the trouble taken.

The true conjugate shown by it is the minimum available. There may be more room but there is at least the amount shown and in most cases the margin of safety is obvious.

Those who wish to experiment with low-power sets are reminded that every case of contracted pelvic inlet can be recognized at the first antenatal examination and that at this time it is easy to secure clear skiagrams. It is remarkable that so much pelvimetry is done in the later months of pregnancy, for, apart from the gain in simplicity and clarity of films taken early in pregnancy, it is surely an advantage to recognize at the earliest date whether Cæsarean section is likely to be necessary and to make arrangements accordingly.

Theoretical considerations.—A modification of the original and long-abandoned mathematical method is employed, the same formula being used as in cephalometry. The objection to this method arises in the variable tilt of the pelvis, but it is found possible to secure a fairly uniform tilt by a modification of the sitting or reclining position (fig. 5).

The patient lies, as shown, with two pillows under the shoulders. A firm support is placed under the lumbar curve (in practice an unopened 1 lb. packet of cotton-wool is used), and the patient is encouraged to exaggerate the lumbar curve as much as possible. The effect on the film of this position, as compared with the simple reclining position, is remarkable and is fairly constant, as judged by Rowden's test (obliteration of the projection of the obturator foramina) or by the position of the tip of the coccyx, which moves from near the shadow of the symphysis to about the middle of the pelvic inlet. The line of the true conjugate, however, cannot be made

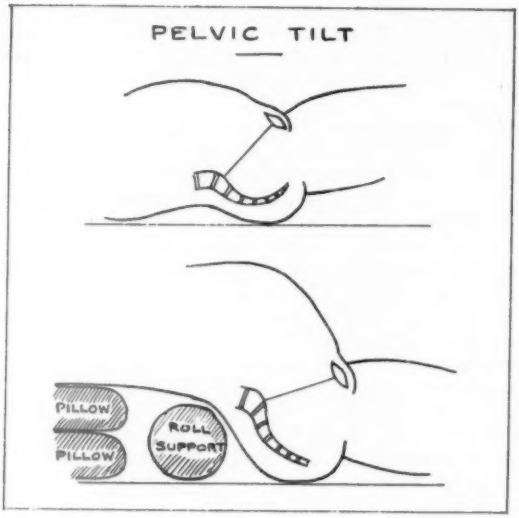


FIG. 5.

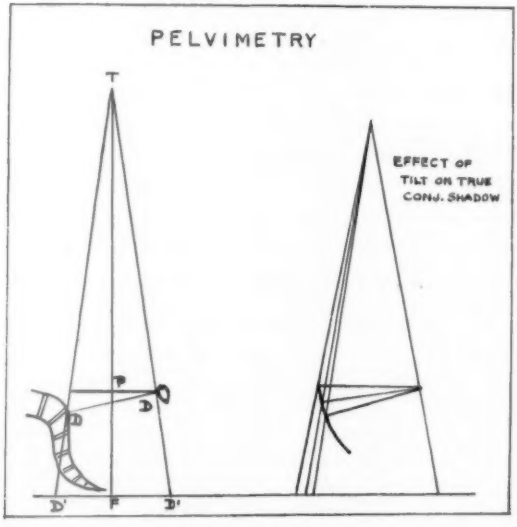


FIG. 6.

Trans. diameter $\frac{D\,D}{D^1\,D^1} = \frac{T\,P + 2}{T\,F}$

True conjugate: $\frac{D\,D}{D^1\,D^1} = \frac{T\,P + 4}{T\,F}$

parallel to the film in this way and the promontory lies usually about 2 in. below the upper margin of the symphysis. By measuring possible projections on a scale drawing, it was found that in the case of the true conjugate the loss of shadow length caused by a tilt of this amount could be compensated for, approximately, by adding 4 in. to the factor T P (fig. 6).

The result of this calculation is likely to be slightly on the low side, especially when the tilt, as can at once be seen, is not very well corrected. If with a very flexible spine, Rowden's test shows the pelvic tilt to have been almost entirely corrected, caution must be exercised and the correction factor reduced to 3 in. or 2 in. There is no difficulty about this, for the obliteration of more of the obturator foramina, as the tilt is corrected, is very clearly seen. In the tilted position the transverse diameter lies about 2 in. below the upper margin of the symphysis and if 2 in. be added to T P the result will be quite accurate.

The method in practice.—With a focus film distance of 30 in. the tube is centred over the symphysis and the distance T P is measured. The tube is then moved 2 in. towards the patient's head and the exposure made. The projection of the true conjugate is then measured on the film and the formula applied (actually the result is read off the table). If the film is not very clear the promontory can usually be defined by following the upper curves of the first sacral foramina.

For the transverse diameter, Stude's obstetric transverse (about $1\frac{1}{2}$ in. in front of the promontory) should be measured. This is usually not the widest transverse measurement but in a flat pelvis it gives a better idea of the room available. The calculation is then made, adding 2 in. to T P as stated above.

This method of pelvimetry takes some time to describe, but in practice the film can be taken in five minutes or less and the diameters can be decided in less than a minute.

APPENDIX

Abridged Directions for Cephalometry and Estimation of Maturity

(1) Patient recumbent on table—palpate fœtal head.
(2) Centre tube over head at focus film distance of 30 in. Measure T P.
(3) Expose and develop film.
(4) Measure short axis of head shadow. D^2 D^2.
(5) Add P H factor to T P, according to size and type of shadow—usually $1\frac{1}{2}$ to 2 in.
(6) Read off result on table.
(7) Make the necessary adjustment to obtain the bi-parietal diameter.

To Obtain Correct P H Values.

	Types of shadow									
							Circular			
	Plan in.		Lateral in.		Oval in.		Occ. post. in.		Occ. ant. in.	
P H near term ...	2	...	1·75	...	2	...	3	...	2	
P H at 32 weeks ...	1·25	...	1·3	...	1·25	...	2·25	...	1·5	

Adjustment of Result.

In case of plan shadow: Result = bi-parietal diameter.

True lateral shadow: Result = sub-occipito-vertical. Add 0·25 near term: 0·2 near 32 weeks.

Oval shadows: Add 0·1 near term: 0·08 near 32 weeks.

Circular type shadows.—True circle: Diameter = bi-parietal. Near circle types:—

(1) If long axis ends where spine joins head, then short axis = bi-parietal.

(2) If short axis ends where spine joins head then: (*a*) If spine shadow stops sharply at head shadow then short axis = sub-occipito-vertical—make correction to bi-parietal as in lateral; (*b*) if spine shadow enters head shadow, then length of short axis lies between sub-occipito-vertical and bi-parietal. Correction approximate only.

Table of Formula Results

Measurement on film in inches	Distance in inches from tube to head as palpated + addition to axis centre. (P H)								
	20 in.	20½ in.	21 in.	21½ in.	22 in.	22½ in.	23 in.	23½ in.	24 in.
3·5	2·3	2·4	2·45	2·5	2·56	2·6	2·68	2·74	2·8
3·6	2·4	2·46	2·5	2·58	2·6	2·7	2·76	2·8	2·88
3·7	2·47	2·5	2·59	2·6	2·7	2·76	2·8	2·89	2·96
3·8	2·5	2·59	2·66	2·7	2·78	2·85	2·9	2·97	3·0
3·9	2·6	2·66	2·7	2·79	2·86	2·9	2·99	3·0	3·1
4·0	2·66	2·7	2·8	2·86	2·9	3·0	3·06	3·1	3·2
4·1	2·74	2·8	2·87	2·94	3·0	3·07	3·14	3·21	3·28
4·2	2·8	2·87	2·94	3·0	3·08	3·15	3·22	3·29	3·36
4·3	2·87	2·94	3·01	3·08	3·15	3·22	3·29	3·37	3·44
4·4	2·93	3·01	3·08	3·15	3·23	3·3	3·37	3·45	3·5
4·5	3·0	3·07	3·15	3·22	3·3	3·37	3·45	3·52	3·6
4·6	3·07	3·14	3·22	3·29	3·37	3·44	3·53	3·6	3·68
4·7	3·13	3·21	3·29	3·37	3·44	3·52	3·6	3·68	3·76
4·8	3·2	3·28	3·36	3·44	3·52	3·6	3·68	3·76	3·84
4·9	3·27	3·35	3·43	3·5	3·59	3·67	3·75	3·84	3·92
5·0	3·33	3·42	3·5	3·58	3·66	3·75	3·83	3·92	4·0
5·1	3·4	3·48	3·57	3·65	3·74	3·82	3·91	3·99	4·08
5·2	3·47	3·55	3·64	3·73	3·81	3·9	3·99	4·07	4·1
5·3	3·53	3·62	3·71	3·79	3·88	3·97	4·06	4·15	4·23
5·4	3·6	3·69	3·78	3·87	3·96	4·05	4·14	4·23	4·32

Estimation of Fœtal Maturity.

Bi-parietal diameter = 3·75 in. at term.

Allow $\frac{1}{10}$ in. per week for growth: e.g. if bi-parietal diameter = 3·5 then there should be 2½ weeks before full term is reached if baby is to be of average size.

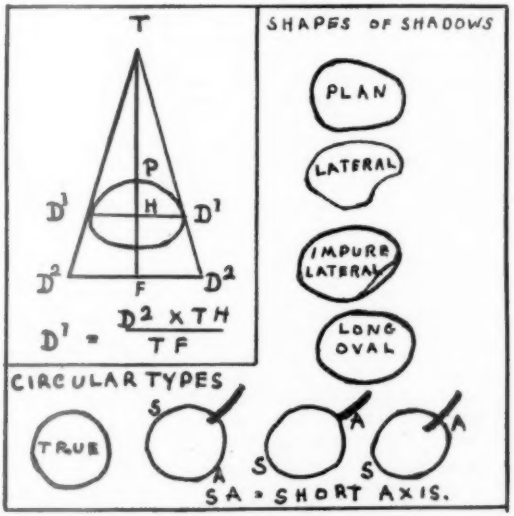


Fig. 7.—Formula used and shadow types.

Discussion.—Dr. R. E. ROBERTS: Dr. Reece's paper opens up for discussion two very important questions, clear answers to which will be of considerable help both to obstetricians and radiologists. The first question is "How far can radiology be relied on to estimate the diameters of the maternal pelvis and of the fœtal skull?" If it can be shown that radiological pelvimetry and cephalometry are reliable, the next question which arises is "How far are such measurements of clinical value to the obstetrician, with special reference to the estimation of the maturity or period of gestation of the fœtus, and in diagnosing the presence, or otherwise, of disproportion?"

The best known and simplest methods of radiological pelvimetry (amongst many others) are probably those of Thoms, Rowden, and Roberts. In each of these great care is taken to posture the patient so that the pelvic brim is parallel to the film, and to arrange the X-ray tube so that the central ray passes through the centre of the brim, and at right angles to it and the film. In the resultant radiograph the brim is seen as a slightly enlarged, but true and undistorted, representation in which all the diameters are enlarged uniformly. From the film image of the brim so produced, different methods are employed by these three workers in estimating the true diameters of the brim, but in all of them the result can be regarded as extremely accurate.

Admittedly, especially in the case of advanced pregnancy, efficient apparatus is required for the production of a readable picture, and for this reason Dr. Reece's plea for the early radiological pelvimetry of patients rather than in the later months of pregnancy, is to be endorsed. But even with the largest of patients it should not be impossible to supply the information required with apparatus of the standard of efficiency supplied by most firms nowadays. The plea that the older and more accurate methods of pelvimetry are not applicable with the presumaby inefficient type of apparatus which Dr. Reece describes as "any cottage-hospital X-ray set," is not, in my opinion, sufficient justification for introducing a further pelvimetric method, such as that which Dr. Reece has this evening described, which cannot be regarded as either reliable or accurate. The absence of a definite standard position of the pelvic brim in relation to the X-ray film must inevitably lead to errors in the result. The adoption of such a method, merely on the plea that it can be performed by "any cottage-hospital X-ray set" will tend to bring the science of X-ray pelvimetry, at present an exact one, into disrepute, and cannot therefore be encouraged.

Except that there is no necessity to posture the patient in the "sitting" position used in pelvimetry, the principles of the methods employed by different workers for radiologically assessing the diameters of the fœtal skull are very much the same as those used in pelvimetry. Either the false centimetre grid of Thoms, or the false centimetre scale of Rowden, or the geometric principle of Roberts may be employed. The difficulty is that, whilst, in pelvimetry, the pelvic brim is in a standard relation to the film, the diameters of the skull are often far from easy to orientiate with any degree of precision. In the case, for instance, of the occipito-frontal diameter, which is the one commonly measured, the degree of obliquity of this diameter to the film may be such that grave possibilities of error may arise in any attempt to assess its true measurement from its film representation. If it lies transversely, and therefore parallel to the film, with the patient in the supine position, its measurement can be accurately performed. If it lies obliquely it may be difficult to make the correct allowance for the tilt, and the result will be considerably less reliable.

Distortion due to obliquity of those diameters which are included in Dr. Reece's "greatest circular section," however, will not be nearly so great as in the case of the occipito-frontal diameter. Dr. Reece is to be congratulated on his appreciation of this fact, and on the application he has made of it in his method of deducing the measurement of the bi-parietal diameter from that shown on the film. I have always felt that except in certain favourable positions of the fœtal skull the radiological mensuration of the occipito-frontal diameter do not reach the same degree of precision as the measurements of the pelvic brim. Dr. Reece's paper has introduced a further cephalometric method which should be of more universal application than those previously described. One must, however, remember that whilst in the average skull the various diameters may bear a definite relationship to each other, variations may occur in any individual case.

Concerning the clinical application of the results of radiological pelvimetry and cephalometry, there must be a considerable diversity of opinion. Pelvimetry alone is often of little value unless accompanied by cephalometry. The finding of normal brim measurements does not necessarily ensure a normal delivery, for just as much difficulty may be experienced in

the passage of a large child through a normally-sized pelvis as of a normally sized child through a contracted pelvis. The demonstration of a contracted pelvis by radiological methods would of course serve to sound the desired note of warning, but the demonstration of a normal pelvis should be accompanied by the demonstration of a normal or small skull if it was to be of full value. Even where disproportion was shown by radiological methods to exist, unknown factors such as the strength of the uterine contractions, the degree of skull moulding, etc., which might occur, could not be foreseen. All the radiologist can do is to supply the obstetrician with information, which can be regarded as reliable, regarding the size of the pelvis and of the fœtal skull; it is then obviously the duty of the obstetrician to make what use he can of the information supplied.

A consideration of pelvimetry would be incomplete without reference to the measurement of the pelvic outlet. As a rule this is readily measurable by clinical methods. In cases of doubt or difficulty, however, it is a matter of ease to estimate radiologically the transverse diameter of the pelvic outlet by the method of Chassard and Lapiné, or the anteroposterior diameters by application of the principles employed in measuring the brim by Thoms, Rowden, or Roberts.

It should also be mentioned that a lateral radiographic view of the pelvis is often of value in demonstrating the general shape of the pelvis, with special reference of course to the posterior surface of the symphysis pubis and the anterior surface of the sacrum.

A set of three radiographs, prone, supine, and lateral, would often give an indication as to the presence or absence of disproportion without recourse to pelvimetry and cephalometry.

With regard to the estimation of the period of gestation of the fœtus by radiological methods one may say emphatically that when a discrepancy is found to exist between the period of amenorrhœa and the size of the uterus, and the period of gestation is in doubt, valuable information may be obtained from a radiological examination.

Not only can the presence of multiple pregnancy, fœtal abnormalities, etc. be sometimes dramatically demonstrated, as being the cause of hydramnios, but a consideration of the normal fœtal shadow (preferably with the patient in the prone position), especially if combined with fœtal cephalometry, will, in the majority of cases, give information as to the period of gestation which is considerably more reliable than that available from clinical methods.

In regard to cephalometry alone, one must, however, introduce a word of caution. In estimation of the fœtal maturity from cephalometric measurements alone, the assumption has to be made that the fœtal head is of the average size for its age. In the majority of cases this assumption is justifiable, but in any particular case one must bear in mind the possibility of a variation from normal in one or other direction. However, from experience one can say that where any element of doubt as to the stage of maturity exists, the radiological estimate can, in most cases, be relied on within a week in either direction. This is well borne out by Dr. Reece's experience, based on cephalometric estimation of the bi-parietal diameter alone. If in favourable cases direct measurement by means of X-rays of the occipitofrontal and other diameters is made, and the general size and stage of development of the fœtal parts are also considered, even a greater degree of exactitude should be possible in future.

Dr. L. A. ROWDEN said that he would confine his remarks more particularly to pelvimetry. The method which he would demonstrate did not require any mathematical tables or formulæ, nor did it require calipers, measurements, or manipulations. He insisted on a tube-film-distance of at least 4 ft. 6 in.; one of 6 ft. would be better still, if reasonable accuracy were to be obtained. The accompanying illustration (see fig. 1) showed the position of the patient and the tube. The patient sat comfortably on the Potter-Bucky, preferably of the "Sectogrid" type, with her back resting on a bed-rest at an angle of 57 degrees to the horizontal plane. In this position the plane of the pelvis would, in ordinary cases, be practically horizontal, as proved by the ascending and descending rami of the pubic bones being superimposed, and the obturator foramina being invisible in the picture. The tube was centred beforehand.

To obtain a clear view of the whole of the pelvic brim it was essential that the anterior portion of the abdomen should be shaded off from the rays so that it would get only

one-third—or less, according to the stage of pregnancy—of the exposure of the posterior portion. He advocated that all women should have the pelvic-brim measurements taken in the early months of pregnancy. It only had to be done once in a lifetime. Whenever considered necessary, the presentation, position, and size of the fœtal head should be ascertained a fortnight before full-term.

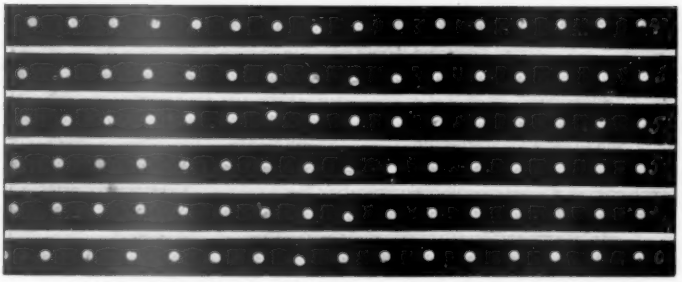
He also thought that this position was the best for determining the relative measurements of the head to the brim. The size of the head would be slightly exaggerated, but this could be easily allowed for.

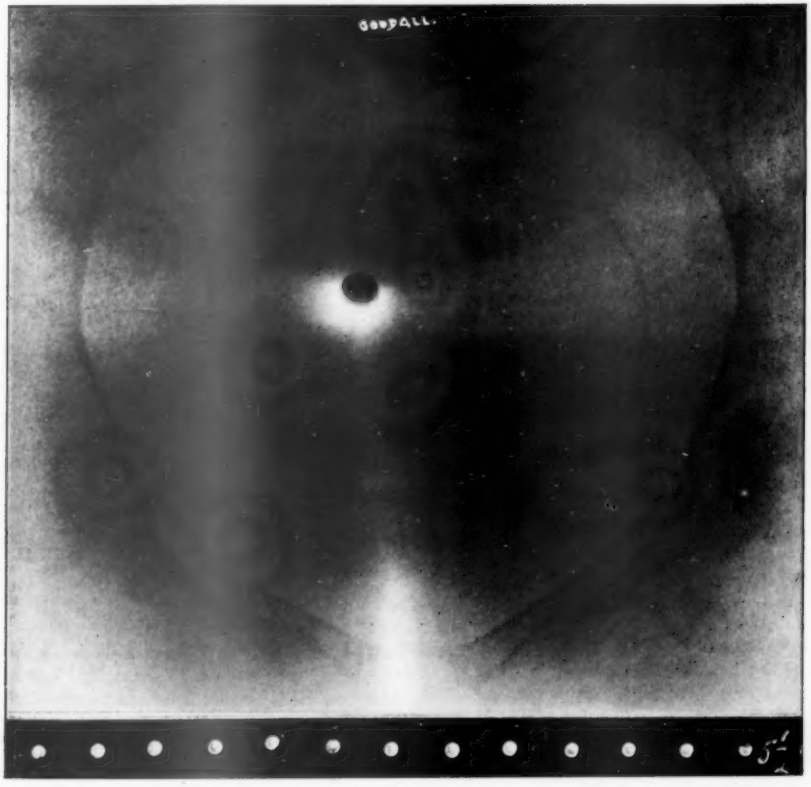
The actual measurements were read off from a series of scales kept in stock, the appropriate one being attached to the picture (see fig. 2). The small dots on these scales

FIG. 1.

represented half-inches at different planes above the Potter-Bucky surface from 4½ to 5½ in. at quarter-inch intervals, the former being the lowest and the latter the highest he had come across (see illustration). It was not really necessary to measure this "pubic distance" from the surface to the top of the symphysis pubis, as it varied with the height of the patient. For example, if the patient was 5 ft. 6 in. in height, the scale representing a pubic distance of five-and-a-quarter could be chosen and the error would, in the pelvic brim measurements, not be more than a very small fraction of an inch.

[Dr. Rowden showed by an experimental brim that the tilting of the pelvis up to ten degrees from the horizontal had practically no influence on the measurements and could be easily allowed for.]





Pubic measurement = 5½ inches.
A - P = 5 inches.
Lat. = 5½ ,,
R. obl. = 5½ inches.
L. obl. = 5½ ,,

Age 26 Height 5 ft. 5 in.
Primipara.
Single fœtus.
Head presentation.
Spine to right.
Occipito-posterior.
33 weeks pregnant.

Dr. JAMES YOUNG said that in regard to radiography, it would almost seem that, as often happened in modern life, science was advancing more rapidly than practice. The evidence that had been presented strongly suggested that from radiographic methods a considerable amount of accurate information could be obtained in regard to the pelvis and the fœtal head, the importance of which the obstetrician was in many cases failing to recognize. He had been particularly impressed by the demonstration of Dr. Reece, and he hoped at an early date to have an opportunity of carrying out investigations along these lines at the British Post-Graduate School.

Dr. REECE (in reply to Dr. Roberts' and Dr. Rowden's criticism of the simple method of pelvimetry described) said that while he agreed without question as to the obviously greater merits of their exact methods, yet he thought it a counsel of perfection to insist that small hospitals should scrap their low-powered sets or give up the idea of pelvimetry. He hoped that his paper had made it clear that a cottage-hospital set could be of great clinical value until a more powerful set could be obtained. He wished again to stress his view that post-maturity should not be allowed, and that only by cephalometry could scientific control of the duration of pregnancy be made possible.

Section of Dermatology

President—HENRY MACCORMAC, C.B.E., M.D.

[*December* 20, 1934]

Mycosis Fungoides.—R. T. BRAIN, M.D., and I. MUENDE, M.B.

M. F., a married woman, aged 60, with a history of occasional irritation, soreness, and swelling of left side of vulva for about a year, was seen by a gynæcologist, who found a chronic inflammatory condition with lymphatic œdema, and referred her to the Whitechapel Clinic on February 24, 1934. There she was seen to have gross œdema of the left labium majus and an inflammatory state of the skin extending to adjacent areas, with some small superficial sinuses. The inguinal lymphatic glands were slightly enlarged; moderate cervicitis was the only other pathological feature. The Wassermann and Kahn reactions were negative at this date and again a month later. Pus from the cervix was not gonococcal, although reaction to the gonorrhœa-fixation test was positive on three occasions. She was given otarsan gr. 1½ o.m., and had routine treatment for the cervicitis. The possibility of lymphogranuloma inguinale was considered, but reaction to a skin test with Frei's antigen was negative. On May 4 an erythematous rash was noted on the neck, upper trunk, and flexures of the arms, and the local lesion continued to spread.

On December 3 she was seen at St. John's Hospital, and a biopsy was performed. At that time moderate œdema of the left labium majus was noted, and moist dermatitis of the vulva, perineum, and gluteal cleft. The affected surface showed slightly raised bosses, up to 2 in. in diameter, having a moist red granular appearance. On the buttocks some of these bosses were in contact across the gluteal cleft, like condylomata, and the pattern was made circinate and irregular by areas where the surface was flat or sunken, as though by atrophy or fibrosis. The inguinal glands were moderately enlarged, firm, and discrete. The patient's husband and her eight children are well. Two children died from unknown causes, at the ages of 19 years and 13 months respectively.

No bromide or iodide has been taken.

Histological report.—There is marked acanthosis with a high degree of intercellular œdema. The stratum granulosum is absent, and the stratum corneum replaced by parakeratotic cells. The intercellular spaces in the epidermis are seen to contain numerous polymorphonuclear and lymphoid cells.

The papillæ are greatly widened, and the tissue of the pars papillaris and upper half of the reticularis shows a marked œdema, with dilatation of the blood and lymph vessels. The corium in this zone is heavily infiltrated by numerous small round cells, most of which are plasma cells, large lymphoid cells, neutrophil and also eosinophil leucocytes, and the endothelial cells show some proliferation.

The histological appearances are strongly suggestive of mycosis fungoides.

Blood-count.—W.B.C. 10,800. *Differential*: Polys. 79%; lymphos. (small 12, large 2), 14%; large monos. 6%; eosinos. 1%.

Discussion.—Dr. J. T. INGRAM asked whether antisyphilitic treatment had been tried.

The PRESIDENT said that though the sections were not characteristic for mycosis fungoides, he did not think they suggested a syphilitic lesion. The appearance of the tumours, however, was characteristic of mycosis fungoides. On Tuesday he had had at hospital a case of what he thought to be typical mycosis fungoides, premycotic lesions and commencing tumour formation, and that patient also had no itching.

Dr. BRAIN (in reply) said that the preparation known as otarsan, which had been given to the patient, was the English equivalent of stovarsol.

He was indebted to Dr. Anwyl Davies and Dr. A. King of the Whitechapel Clinic for this case.

? Pityriasis Lichenoides: Case for Diagnosis.—R. T. BRAIN, M.D.

A. H., boy, aged 8, attended the Hospital for Sick Children, Great Ormond Street, December 5, 1934 with a history of a rash on his back for seven days. His mother had a suspicion that this was due to a Schick test which had been performed three weeks before the eruption appeared. Irritation was slight.

The eruption was limited to the trunk and adjacent parts of the limbs. Many of the lesions were pale pink in colour and oval in shape, and had a scaly surface. These features suggested pityriasis rosea, but no herald spot could be found; many macules were dotted between the papules and the scales were dry and adherent, as in psoriasis, on some of the smaller papules.

The Wassermann and Kahn reactions were negative.

The eruption has persisted with little change in the individual lesions, but these are more numerous on the neck and are, in fact, almost confluent. A few papules have appeared on the scalp also.

Discussion.—Dr. G. B. DOWLING said that the position of this case was about half-way between guttate parapsoriasis and pityriasis lichenoides acuta.

He recalled the fact that, shortly before cases of the latter condition were first seen in this country—Dr. A. M. H. Gray having demonstrated the first example—there had been a small number of cases similar to the one under discussion. The President had shown the first and had pointed out at the time that, while he regarded it as a variety of guttate parapsoriasis or pityriasis lichenoides chronica, the prognosis was much more satisfactory, as in most cases the condition cleared up spontaneously in a relatively short time.

Dr. A. M. H. GRAY said that he agreed with Dr. Dowling, but he did not see why there should be a differentiation between pityriasis lichenoides chronica, and pityriasis lichenoides varioliformis et acuta, as eventually they might run into one another. In the case now shown there were no necrotic lesions at present; it might remain an ordinary chronic case.

Dr. I. MUENDE thought this might be the congestive type of pityriasis rosea. There was a patch on the side of the neck which had lasted three weeks, and there was definite adenitis. It might be worth while to wait three weeks to see what happened.

Morphœa.—J. E. M. WIGLEY, M.B.

An apparently well developed, healthy girl, aged 14½, has had this eruption for about four years. It first appeared on the back of the neck, then on the shoulders, arms and legs, then on the trunk, and lastly on the forehead, always symmetrically. There is marked itching when she gets hot.

There is an area of thickened and atrophic skin, roughly rectangular and about 4 in. by 3 in. in size, just below the nape of the neck. The remainder of the eruption consists of atrophic spots, with a definite lilac-coloured border, and an ivory-tinted surface, arranged with remarkable symmetry, on the forehead, the shoulders, the forearms, the upper abdomen, and the thighs. There are no lesions to be seen in the mouth. Otherwise, physical examination is negative. The Wassermann reaction is negative.

The differential diagnosis lies between morphœa and atrophic lichen planus, but I think that the points I have enumerated support the diagnosis of morphœa guttata or "white spot disease."

Discussion.—Dr. F. PARKES WEBER said that a more or less symmetrical dermatosis which was distributed like rain drops over a considerable region ought not to be called morphœa, as morphœa was limited to patches, and often the patches were segmental; hence the frequent use of the qualifying term "zoniform." He agreed that this case belonged to the large group of atrophodermia guttata, and it was not of segmental grouping.

The typical cases of "white spot disease" which he had seen were characterized by a striking mother-of-pearl-like surface, and he thought the term "white spot disease" should be limited to cases which showed that mother-of-pearl appearance, the distribution being mainly about the shoulders and neck.

Dr. MUENDE said it was difficult to agree with Dr. Parkes Weber's remarks and to associate the term scleroderma with this case, as there was no hardness, it being in the nature of an atrophic condition. The striking point was that these lesions were associated, in the early stage, with a little hyperkeratosis, which one never saw in a sclerodermic condition. For that reason he thought it more probable that this was atrophic lichen planus.

Dr. J. T. INGRAM said there was something at the back of the neck which was not atrophy; there was scleroderma or thickening of the skin. Was it generally agreed that one occasionally found hyperkeratosis with scleroderma? Was the condition in this case likely to clear up completely? Scleroderma in young people usually cleared up.

The PRESIDENT wondered whether there was any way of distinguishing between white spot disease associated with scleroderma, and lichen planus followed by guttate atrophy. He had seen in both conditions a form of white spot disease, the nature of which could only be identified by an associated lichen planus or morphœa, and he had shown before the Section cases which illustrated that point. In both conditions the white spots were similar end-results which gave no clue to the primary lesion.

Low-fat Dietary Treatment of Psoriasis.—H. C. SEMON, M.D.

A synopsis of the Grütz-Bürger conception and treatment of psoriasis appeared in the *Lancet* of September 15 last; pp. 605-6, and was extracted from their original paper "Die Psoriasis als Stoffwechselbroblem," *Klin. Woch.*, 1933, xi, 373.

Very briefly these authors attribute the disease to a dysfunction of the lipoid metabolism in the blood and cutaneous tissues, and are at the present time undecided as to whether the disturbance must be regarded as due to a quantitative increase or a qualitative alteration in the chemical constituents concerned. It has long been known that psoriasis scales contain an excessive proportion of cholesterin, one of the lipoids in question, and it was this fact that started Prof. Grütz on his researches. It is true that other investigators (e.g. Puley and Brill) had previously examined the blood of psoriatics from this standpoint, but they had contented themselves with one or two fortuitous blood specimens, from which no suggestive information was obtained. Grütz and Bürger on the other hand devised a "tolerance test" on the same lines as that in general use now for diabetes, etc., and their results, which have not as yet been contradicted so far as I am aware, are at least suggestive. 5 grm. of cholesterin in 100 c.c. olive oil are administered to the patient, fasting, and the blood for investigation (50 c.c.) is withdrawn at 4, 8 and 24 hours' interval thereafter. It is claimed by the authors that the average increase of lipoid fractions determined biochemically in psoriasis as compared with non-psoriatic cases is 42%.

The number of cases on which this statement is based is admittedly small—only 21—but the results were uniformly consistent, and are supported by the results obtained by Dr. Harry Coke in the three cases I have so far been able to submit to him.

We can formulate no opinion on so small a material, but when considered in the light of the clinical response to treatment, the findings are of interest. The treatment consists in reducing the fat intake to a minimum. Grütz states it must not exceed 20 grm. (2/3 oz.) per diem in the case of the adult and half that quantity in the child.

A dietary based on these principles has been compiled by Miss Clendinnen, the dietitian at the Royal Northern Hospital, and the two cases now shown have been under its influence since the beginning of October.

I. C. B., female, aged 63, married. History of psoriasis following a "dermatitis" of the legs in 1914. Never quite free from the eruption, which had been getting steadily worse for the last two years, and was practically universal when she was admitted to hospital October 7, 1934. The face, neck, body, arms, and legs were thickly covered with indurated nummular plaques of the disease, and the brawny induration of the forearms was so marked that for the first month of her stay in hospital it was impossible to locate a vein for the serum test. Removal of her clothes resulted in thick showers of scales, and the bed-linen was always thickly sprinkled with them. The case was, in fact, approaching the stage of generalized exfoliative dermatitis. No other treatment—except occasional baths (non-medicated) for the sake of cleanliness, and an occasional application of zinc cream for cracked and fissured areas—has been allowed to complicate the dietary measures which have been strictly enforced for a period of three months. She has lost 6 lb. in weight.

II. E. B., a girl aged 9. The effect of the treatment in this case, although quite definite, has been rather disappointing when compared with that obtained in Case I. She was admitted to hospital on October 6, 1934, with small thickened nummular patches of psoriasis on the forehead, scalp, back, and legs. She is said to have been affected for two years; the manifestations began on the left side of the forehead following sepsis in that situation. Under the dietary measures the plaques have become much paler and less scaly, but they have not cleared to anything like the same extent as those in Case I have done; those on the scalp have cleared least of all. Her serum lipoids on the other hand were found more atypical in the tolerance test than those of Mrs. B. (*see* chart). It was brought to my notice yesterday that in spite of my strict instructions, a good deal of chocolate has been given to the child by friends and others in the ward, and this may possibly account for the delayed clearance of the lesions. She has gained 1 lb. in weight.

Discussion.—Dr. HARRY COKE said that after the stimulation provided by the leading article in the *Lancet* (ii), Sept. 1934, Dr. Semon asked him whether it would not be possible to attempt a confirmation of the results put forward by Grütz and Bürger. With regard to these, there were one or two criticisms that one should not fail to bring forward. The conclusions that these workers reached were based on "average" findings on a small number of cases, and the standard deviations were sometimes even bigger than the changes on which the conclusions were based. It was not necessary to enlarge upon the sources of error involved by taking average results in this manner without paying any attention to the individual cases.

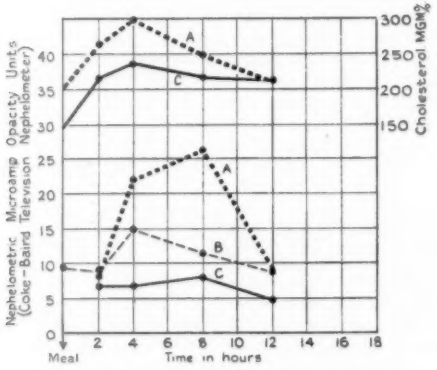
The next point of practical importance was that the investigations suggested involved serial estimations in six specimens of blood of total fat, lipins, and differential cholesterol content, and for this they required 50 c.c. blood from the patient six times in twenty-four hours; and therefore for such reasons as these, coupled with the fact that time was an important consideration, a replica of their experiments was considered beyond the present scope.

It was then open to deliberation as to whether it was not possible to attempt something similar, that could be simple, and without too much discomfort to the patient. He (Dr. Coke) therefore turned to the simplest known fact, namely, the increase in opacity, milkiness, or lipæmia, after a meal rich in fats. A state of lipæmia of the blood had often been observed

and noted, especially in association with diabetes, xanthomatosis, nephrosis, lipoid histiocytosis, and the pseudolipæmia sometimes present in acute leukæmia. These had been single, and often uncontrolled, observations, and had rarely been measured accurately, and almost certainly not used as a basis of measurement in a serial test comparable to the glucose tolerance tests. The procedure was as follows: The patient was starved of fat and cholesterol for twenty-four hours. Then a test-draught of 5 grm. of cholesterol in 100 c.c. of olive oil was given. (The equivalent amounts might be made more palatable by emulsifying the oil with the cholesterol dissolved in it.) 8 c.c. of blood were then removed with a Behring venule at 0, 2, 4, 8, and 12 hours after. After clotting, the serum was removed, and the opacity measured very quickly by means of a special photo-electric nephelometer. The opacity of the serum could be read off directly on the micro-ammeter, and this method overcame the counter-estimations necessary with visual nephelometers due to the yellow colour of the serum.

[The results obtained are seen in the chart below.

In this graph the ordinates form the time at which the blood was removed in relation to the test-draught, and the abscissæ, the opacities as measured in micro-amp. units.



A.—E. B., aged 9. Original psoriasis. Untreated.
B.—Mrs. C. B., aged 63. Psoriasis, under treatment.
C.—Case of lupus vulgaris, as comparative control.

The lowest curve is that of a person with lupus vulgaris, and is significantly horizontal, despite the large amount of fat with which the organs had to deal. On the other hand, the highest curve is that of the girl, suffering with generalized psoriasis, who was shown to-night, taken under the same conditions. The middle curve is that of the woman, who is also present this evening, although it was taken some six weeks after treatment had commenced, because the psoriatic lesions were so extensive in the beginning as to make it impossible to obtain the blood satisfactorily. In the upper part of the figure is the corresponding cholesterol estimations of the first two curves.]

The differences noted were considerable, and one might say also that they were encouraging, but it should be clearly understood that they were shown only for the purpose of indicating a practical, simple and efficient line of attack; and that the results obtained and shown on the graph were to be considered merely as "observed facts"—that is to say, one could not and must not draw any conclusions from them in this embryonic stage, nor did he put forward such results as holding in any way a "brief" for the conclusions arrived at by Grütz and Bürger.

Dr. GORDON said that he had had two patients for whom he had felt that the method might be tried, but 100 c.c. of olive oil was a meal they would not face. They said they preferred the psoriasis to the diet.

Dr. JOHN BODMAN said that he had tried the use of intramuscular injections of 1 gramme of cholesterol dissolved in 20 c.c. of olive oil; this was more easily tolerated than the large doses of oil by the mouth.

Dr. W. S. W. GUTHRIE said that the claims of Grütz and Bürger (*Klin. Woch.*, 1933, xii, 373) should be thoroughly investigated, as, in one or two respects, the results given were not convincing. It was true that the chemistry was very advanced, but the way in which the results were tabulated and the argument set forth made it appear that a special cause was being pleaded. The figures for total fat and for cholesterol content of the serum in their normal controls and psoriatics were given as averages for the fasting values, and at 4 hours, 8 hours, and 24 hours, as percentage increases over the average fasting levels. Average values meant little over a small series of cases. He (the speaker) plotted out the average absolute values fasting and at 4, 8 and 24 hours, calculated from their data. The result was that the fasting levels for total fat and cholesterol were certainly higher in psoriasis, but as there was a smaller percentage increase in the later specimens of serum from patients with psoriasis than in normal people, the curves took a closely parallel course.

In a later paper by Grütz (*Arch. f. Dermat.*, 1934, clxx, 143) an illustration was given of a section of a psoriasis lesion in his patient with coexistent psoriasis and xanthoma diabeticorum. Stained with Sudan III and hæmatoxylin, it showed the features which had been mentioned by Dr. Semon. Sections stained by Sudan III from cases of uncomplicated psoriasis failed, however, to show this fatty infiltration spreading outwards from the papillæ through the epidermis to the parakeratotic stratum corneum. Grütz concluded, in rather surprising fashion, that in these typical cases of psoriasis, fatty substances did escape in excess from the capillaries, but the amount was not sufficient to be shown by the usual staining methods.

For these reasons it seemed advisable to regard Grütz's claims with considerable suspicion.

Dr. I. FREUDENTHAL said that a dermatologist at a Breslau hospital, who had himself severe psoriasis for many years, had tried a fat-free diet without success.

Dr. SEMON (in reply) said that the clinical results both in the cases shown and in several private patients had been, he thought, sufficiently encouraging to warrant a more extensive trial. On one point he was satisfied—in none of the cases had there been (or developed) a tendency for the disease to spread, or become inflamed or exfoliative in character. Rather the reverse, and there might be a useful future for the treatment in combination with the accepted local applications, which had justified themselves therapeutically over years of trial.

Lichenification.—F. PARKES WEBER, M.D., and F. JUPE, M.D.

The patient is an Englishwoman, aged 61, a widow, who has suffered from a pruriginous dermatosis of the lower limbs since the age of 6 years. At that time she was in India, and it had been attributed to bathing in the Ganges or to mosquito bites, but since coming to England, at the age of 11 years, it has not decreased but considerably increased in extent. The elementary lesions seem to have been smooth, reddish, flat papules, which became confluent over a great part of both legs up to the knees, the skin over this region being now thickened and hard, with scabs from scratching here and there. The dorsal surface of both feet shows papules and patches, which have not become confluent. No other parts of the body are affected, excepting that there are some red shiny papules (resembling lichen planus) over the outer posterior part of the right thigh, which have developed during the recent years. In her girlhood the eruption was limited to the skin over her shins, so the patient tells us.

She is somewhat fat, and has permanent high blood-pressure (about 210/90 mm. Hg), but seems to enjoy fairly good general health and presents no signs of any other disease. Blood-count (October 31, 1934): Hb. 80%; erythros. 4,300,000; leucos. 8,100 (eosinos. 3%; basos. 1%; polys. 49%; lymphos. 35%; monos. 12%). The

blood-serum gives negative Wassermann and Meinicke reactions. The lymph-glands in the groins are very slightly enlarged, but the patient says that when she was a girl there was sometimes a swelling in the groins as large as a hen's egg.

Microscopical examination, by Dr. I. Muende, of a lesion removed from the skin of the right thigh above the knee. Epidermis: There is a marked increase in thickness of the stratum corneum with a corresponding hypertrophy of the stratum granulosum. Corium: The papillæ are obliterated, with flattening of the epidermo-dermal junction as a result. The pars papillaris (extending right up to the stratum germinativum) is completely replaced by closely packed endothelial cells, in which are embedded numerous irregularly placed small blood capillaries. Beneath this zone there is a narrow fringe of small round cells.

Diagnosis suggested by Dr. Muende from the microscopic examination: The histological appearances suggest an embryonic angiomatous nævus with superadded lichenification.

Discussion.—Dr. G. B. DOWLING suggested that this was hypertrophic lichen planus, at least from the objective point of view. The development of lesions in a scar (Koebner's phenomenon) was evidence in favour of the diagnosis of lichen planus rather than the alternative prurigo.

Dr. A. M. H. GRAY said he agreed that, clinically, this looked more like lichen planus. What seemed to be most convincing was that some of the earliest lesions were flat, shiny, and pinkish in colour. Also the angular shape of some of the lesions, associated with little pits on the surface, were just like what one saw in lichen planus.

Dr. MUENDE said that although he reported on the section without seeing the patient, he was still inclined to think that the condition was primarily nævoid, which had become lichenified, rather than hypertrophic lichen planus. The histology appeared to bear this out. The replacement of the corium by endothelial cells, through which imperfect blood-vessels took irregular courses, suggested to him an embryonic angiomatous nævoid condition. The history of an onset at six years appeared to support this diagnosis. Recurring attacks of irritation could, in his opinion, account for the lichenification.

Multiple Endotheliomata.—ROBERT KLABER, M.D., and W. LEVITT, M.D.

This patient, who was shown at the last meeting of the Section,[1] has since been treated by moderately hard X-rays. The tumours have almost entirely disappeared under this treatment.

Discussion.—Dr. LEVITT said that he had begun to treat the patient on November 22, 1934. He used comparatively hard rays, 150 k.v., with a 5-mm. filter. The irradiation was planned to give a uniform dosage to all the skin of the face, going just beyond the margin of the hair. After the sixth dose little regression was noticed in the largest tumour, and no change in the others, hence it was obvious that the growths were not of the very radio-sensitive class.

Dr. SEMON asked what effect the dosage given had had on the hair.

Dr. LEVITT (in reply) said that hairs were included in the irradiation effect. Some radio-dermatitis persisted. Unless there was inflammatory reaction in the skin, one did not achieve the best results in carcinoma. In many cases the hair would re-grow; he had not seen a case in which, if hard rays were used, the hair would not grow again.

[1] *Proceedings*, 1935, xxviii (Sect. Derm., 20).

Erythema Induratum (with Darier-Roussy Sarcoids).—ROBERT KLABER, M.D.

This man is a printers' assistant aged 46. He was well till two years ago when he had an attack of measles, followed by a bronchitis which has persisted.

Nine months ago painful nodules appeared on the calves; these were at first subcutaneous and later became more superficial and bluish-purple in colour. Since then similar nodules have appeared in various other areas, especially over bony points.

Two ill-defined tender nodules may be palpable to-day, one just above the right iliac crest and one just above the left olecranon process. Several are present on the left calf; they are more easily felt than seen.

There is no diffuse perniosis, and no ulceration.

Patient also complains of periodic stiffness and swelling of muscles in various regions. This suggests that similar changes may be occurring in intramuscular veins.

The Mantoux reaction is strongly positive, using $\frac{1}{10}$, $\frac{1}{20}$, and $\frac{1}{40}$ c.c. of old tuberculin.

Skiagrams of the chest show slight bilateral basal bronchiectasis.

I have regarded this case as an example of that form of erythema induratum which was first described as the hypodermic sarcoid of Darier-Roussy.

Discussion.—Dr. G. B. DOWLING said that in a long and full discussion on sarcoids held in Strasbourg in July 1934 certain definite conclusions appeared to have been reached. The President (Professor Pautrier) summed up the position by saying that in France there were three definite conditions which were called sarcoid: (1) The miliary lupoid, which in reality was the disseminated follicular lupus of Tilbury Fox. (2) Hypodermic sarcoids of Darier-Roussy. (3) Sarcoid of Boeck and lupus pernio which were one and the same general disease.

He regarded the hypodermic sarcoid of Darier-Roussy as a syndrome, frequently tuberculous, sometimes syphilitic, and sometimes due to other causes. They represented a local reaction of the subcutaneous tissue to blood-borne infections and were not to be confounded with erythema induratum of Bazin, which was always tuberculous, and which tended towards ulceration.

Dr. KLABER (in reply) said he had not seen the paper which Dr. Dowling mentioned. He believed that Schaumann and others had taken the view that Darier-Roussy sarcoid was only part of erythema induratum.

Dr. A. M. H. GRAY said the view Dr. Klaber mentioned was that held by Volk in his article in Jadassohn's "Handbuch." It raised the difficult subject of the ætiology of these nodules. He (Dr. Gray) believed that they might be produced by a variety of irritants, probably bacterial, acting on a suitable soil. There seemed to be evidence of tuberculous infection in this case, but some cases had been recorded in which such was absent. He believed that Guy, of Pittsburgh, produced similar lesions by injecting intravenously dead cultures of coli organisms. He (the speaker) considered that it was a group reaction, not a specific disease associated with a particular organism. There was a little confusion about the presence of subcutaneous lesions in Boeck's sarcoid. Subcutaneous infiltrations occurred in that condition. Some years ago he had had a severe case of lupus pernio in which not only were there many cutaneous lesions, but the whole front of the forearms and the backs of the hands had deep subcutaneous infiltrations; they were not lesions which came out and went, as in the subcutaneous sarcoids and in erythema induratum, but large plaques which persisted in the same way as the cutaneous lesions did.

The PRESIDENT said that this was a male patient and he wondered whether Bazin's disease occurred in that sex. In one supposed case in a male patient the condition had been found to be due to the *Spirochæta pallida*.

Lichen Planus.—L. FORMAN, M.D.

D. B., aged 28. Shown at a previous meeting of the Section.[1] After treatment with arsenic and bismuth, a lichenoid eruption developed, resembling lichen planus and lichen spinulosus, with a network of leukoplakia on the mucous membranes, and a diffuse pigmentation of the skin. Now the eruption has faded and the pigmentation largely disappeared.

There are atrophic bald patches on the scalp and similar atrophic areas on the trunk. On the mucous membrane of the right cheek is a patch of atrophy with a ring of leucoplakia representing one of the original lichen planus-like leucoplakic patches. Shown because of the difficulty experienced when such a patch of atrophy is seen, to determine whether it has been an area of lichen planus or lupus erythematosus.

Kaposi's Disease.—L. FORMAN, M.D.

J. D., aged 56. Two years' history. The eruption began on the small finger of the left hand and slowly extended. Now there is a patch of purplish infiltration of the skin, fairly sharply defined, on the back of the left hand and similar areas affecting the skin of the fingers. No other lesions.

Microscopical examination.—There is fibrosis of the deeper layers of the cutis; dilatation of the capillaries, and there are newly formed capillaries with fibroblastic response in the deeper layers. Deposits of iron pigment are seen in sections stained appropriately.

Dr. F. PARKES WEBER regarded this as a particularly fine example of Kaposi's so-called idiopathic multiple pigment sarcoma; it showed a large blue raised patch on an upper extremity, uncomplicated by other lesions. In such a case the biopsy examination ought to show the real histology of the disease, though that did not necessarily settle its true nature.

The present case was very like early cases shown in England (by Sir Jonathan Hutchinson), characterized by blue swellings in hand or foot. Hutchinson suggested that there was a causal connexion with gout. He (Dr. Weber) was inclined to regard the condition as neoplastic.

Pringle Type of Sebaceous Adenoma.—L. FORMAN, M.D.

F. R., a girl aged 6. Spots have been noticed on the face for the last six months. The patient is the third of a family of five girls, the fourth of whom is epileptic. The father has similar lesions on the face and is mentally deficient.

On the nose and the adjoining parts of the cheeks are numerous tiny reddish brown tumours. On the chin are small capillary nævi.

The association of sebaceous adenoma and other types of pigmented and vascular nævi has been frequently noted.

Discussion.—Dr. R. T. BRAIN said that a case which he had seen at the London Hospital was more typical of Pringle's disease than the present case was. There were more lesions at

[1] *Proceedings*, 1933, xxvi, 997 (Sect. Derm., 51).

the side of the nose, and there was an agglomerate lesion on the forehead, of a verrucose appearance. The patient, a boy, also had epileptiform fits, and his sister had Pringle's disease too, but she had no fits. An association in the same patient of tuberose sclerosis and the skin manifestations of Pringle's disease was not uncommon.

Dr. FORMAN (in reply) said that there might be several factors transmitted in this condition explaining the presence or absence of gliomatous changes in the brain and tumours in the kidney and heart, in different individuals.

Section of Neurology

President—S. A. KINNIER WILSON, M.D.

CLINICAL MEETING, DECEMBER 20, 1934, AT THE WEST END HOSPITAL FOR NERVOUS DISEASES.

Thyrotoxicosis with Unilateral Exophthalmos, Hyperpituitarism, and Infantile Hemiplegia.—C. WORSTER-DROUGHT, M.D.

L. C., male, aged 13 years, first admitted to hospital February 16, 1934, on account of swelling in the neck, and weakness of the left arm and leg.

History of present illness.—In December 1933, after an attack of influenza, the right eye became prominent, and four weeks before admission to hospital swelling in the neck was noticed by the school doctor. Since that time the patient becomes unduly hot on slight exertion.

Previous history.—Full-time child, normal labour. Convulsions at age of 6 weeks. After five weeks in hospital was discharged with left hemiplegia. Fits gradually became less frequent and he has had no attacks for four years. He talked at the age of 3, and walked at the age of 4, in spite of left hemiparesis.

Family history.—Father and mother alive and well. Three sisters aged 28, 25, and 11, and one brother, aged 17. No history of fits, of goitre, or of giantism.

Physical examination.—Cranial nerves: Right-sided exophthalmos with enlargement of palpebral fissure. Left-sided weakness of lower half of face. Deficient pterygoid movement; jaw swings to left; speech jerky and nasal. Tongue deviates to left; slight left-sided palatal weakness.

Uniform enlargement of thyroid gland, with neck measurement of 15 in.; right lobe larger than left.

Left-sided hemiparesis with ½ in. shortening of left arm, and 1 in. shortening of left leg. Slight wasting of both left arm and left leg. Fine tremor of outstretched hands. Knee- and ankle-jerks brisk; left greater than right. Plantar reflexes: right flexor; left indefinite.

Hands large (4½ in. by 7½ in.); feet very large (shoes, size 11). Height 5 ft. 7 in.; weight 8 st. 9 lb.

Heart enlarged to right of sternum. Impulse all over præcordium; venous pulsation in neck. Tachycardia; pulse 130; blood-pressure 136/50. Basal metabolic rate + 100; blood-count normal. Wassermann reaction negative.

X-ray examination shows large and very thick skull with enlargement of the sella turcica.

Patient is intelligent but very excitable and restless.

Commentary.—There can be no doubt that in addition to the thyrotoxicosis there is definite over-activity of the anterior pituitary lobe, as indicated by the large head, thick skull, and large hands and feet. The hemiplegia is presumably due to an attack of polio-encephalitis in infancy. The association of thyrotoxicosis with this type of hyperpituitarism appears to be rare. I have previously recorded a similar case under the heading of "Thyropituitary endocrinopathy in a boy aged 14."[1]

In the case shown, partial thyroidectomy has been advised, but the parents refused operation. Consequently for the past three months the patient has been treated with the preparation di-iodotyrosin, one tablet t.d.s. No noteworthy change has been observed excepting that possibly he is less subject to undue fatigue.

Discussion.—Dr. F. PARKES WEBER said that he regarded this as a genuine case of acromegaly as well as one of hyperthyroidism. He thought the association between Graves's disease and acromegaly was fairly well known, though it was rare. The infantile hemiplegia seemed to be totally independent, and was probably connected with an early attack of polio-encephalitis.

An objection against the new drug mentioned was its great expense. He was treating a case of Graves's disease with it, but, so far, there had been no benefit.

A proposed new treatment for hyperthyroidism was based on the functional connexion between a pituitary hormone and the thyroid gland.

Dr. RUSSELL BRAIN said that the case was a very interesting one, as there was now much evidence that there existed in the anterior lobe of the pituitary a thyrotropic hormone which stimulated the thyroid and produced the symptoms and some of the changes of exophthalmic goitre. It was tempting to relate the clinical evidence of over-activity of the anterior lobe with hyperactivity of the cells which caused the thyrotropic hormone. He asked whether Dr. Worster-Drought had considered applying X-rays to the pituitary.

Dr. P. CLOAKE said this case raised the question of the association of thyrotoxicosis and organic nervous disorders, such as was seen in post-encephalitic states. The association might only mean that certain organic nervous diseases predisposed their subjects to thyrotoxicosis. He wondered whether any member of the Section had seen a similar condition in relation to paralysis agitans. Recently he had seen a patient with tachycardia, slight exophthalmos of the left eye, and paralysis agitans tremor in the left hand; the patient was nearly 60 years old. Her basal metabolic rate was, however, only slightly raised (+ 6).

Dr. WORSTER-DROUGHT (in reply) said he agreed that the hyperpituitarism probably resulted from a chromophil enlargement of the anterior lobe of the pituitary body. There was, however, no interference with the optic chiasma and there was no evidence of progressively increasing adenoma.

Arrangements for deep X-ray applications to the pituitary region had already been made. He agreed with Dr. Russell Brain that it would be of interest to note if such treatment had any effect upon the thyrotoxicosis—in the absence of any X-ray treatment to the thyroid. He (Dr. Worster-Drought) regarded the infantile hemiplegia as merely an accidental association and did not consider that the previous cerebral lesion in any way predisposed the patient to the endocrine disturbance.

Di-iodotyrosin was an organic preparation containing iodine, introduced by Roche, and, having an antagonistic action to that of thyrotoxin, it was said to be of special benefit in juvenile cases.

In reply to Dr. Cloake: He had recently had in hospital a case of paralysis agitans associated with thyrotoxicosis in a woman, aged 58; excision of two-thirds of the thyroid had been successfully carried out. Considerable improvement had resulted in all symptoms of the thyroid disorder, but there was no noticeable effect upon the muscular hypertonia or tremor of the parkinsonism.

[1] *Brit. Med. Journ.*, 1927 (i), 50.

Brown-Séquard Syndrome; Right Hemihæmatomyelia.—T. R. HILL, M.D.

A. L., male, aged 22.

Fracture of body and right articular process of 6th cervical vertebra. Loss of thermal and pain sensation below level of about 4th dorsal segment on left side. Exaggerated deep reflexes: ankle-clonus, and extensor plantar in right leg. Lower motor-neuron weakness of right hand and forearm. Patient originally showed sensory loss over distribution of lower roots of right brachial plexus and a marked right-sided Horner's syndrome. Traces of the latter remain.

Sir JAMES PURVES-STEWART said that he had seen numerous cases of intramedullary hæmorrhage due to war injuries, but, though he had had the advantage of the collaboration of Sir William Thorburn, surgical intervention had usually been avoided unless there was definite clinical or X-ray evidence of something which was causing pressure on the spinal cord, whether by fractured laminæ or by a foreign body. They saw no object in adding the effects of surgical shock to those of military traumatism.

Pituitary Adenoma with Acromegalic Changes in Hands and Feet.—T. R. HILL, M.D.

A. R., female, aged 45.

The acromegalic changes are almost confined to the hands; some changes in the feet. Symptoms began in 1923 with severe headaches which recurred over a period of three years. In 1924 the patient had to have her wedding-ring enlarged. Since 1926 the condition seems to have remained stationary. The headaches declined and little or no advance in acromegalic changes has taken place. Skiagram shows ballooning of sella turcica with thinning of its walls. Visual fields normal.

? Encephalomyelitis: Case for Diagnosis.—E. H. LARKIN, M.B.

R. C., male, aged 7.

Acute illness with sore throat, January 1934, followed by acute otitis media (left); discharge persisted until March. Went to school in March; three weeks later began to walk on tip of toes, with tendency to fall to left side.

Previous history.—Was thrown out of side-car when twelve months old. No injury.

Family history.—Child's mother, who was killed when he was twelve months old, had had a "tuberculous" spine from the age of 4 until that of 7.

13.6.34: Rather ill, with slight temperature (100°).

On examination.—Tendency to fall towards left. Dysdiadochokinesia (left). Can stand with eyes closed but sways a good deal. Papillœdema marked. Babinski's sign positive on left. Left abdominal reflexes absent.

On the following day the temperature was normal. Lumbar puncture: pressure greatly increased; protein, cells. Lange's test: chlorides and sugar normal.

The child was kept in bed for a month. The cerebellar signs remained unchanged. The papillœdema remained constant but the pyramidal signs varied. Occasionally the reflexes were more exaggerated on one side than another; sometimes Babinski's sign was present on either side, or on both sides.

After a month he was allowed out of bed. His gait was very incoördinate, with marked hyperextension of the knees and with the trunk bent forward. A week later the incoördination was so great that he could not walk at all. The papillœdema had increased considerably and now measured several dioptres.

Babinski's sign was present on both sides but the abdominal reflexes were brisk.

After a further week's rest in bed—during which the signs did not change, except that Babinski's sign was sometimes present and sometimes not—the child was allowed out of bed again. Since then he has been up and about.

9.10.34: A complete examination was made. Head-circumference 22¼ in. Papillœdema 1 D. Lumbar puncture: pressure 240 mm. Queckenstedt normal. Cells, protein. Lange's test, normal.

Babinski's sign on left; not on right. Adiadochokinesia on left; not walking at all well; great incoördination and hypotonia.

1.12.34: Moderate improvement in gait and coördination. Head circumference unchanged. Health very good. No definite pyramidal signs (left plantar ? extensor). Left abdominal reflexes slightly less than right. Mild dysdiadochokinesia, left. Papillœdema less than 1 D. Skiagram of skull (19.6.34): No enlargement of sella turcica, but pronounced uneven density of bones of skull.

16.8.34: Skull represents the typical appearance of excessive cranial pressure. Sella turcica normal. Mantoux reaction negative.

Discussion.—Dr. NEILL HOBHOUSE said that this case had been under his charge for five weeks in the summer, and the contrast between the condition then and now was marked. In the summer the boy was definitely ill; he had now improved physically even more than neurologically. He (the speaker) was not satisfied that the hydrocephalus was a recent event; from the X-ray appearance he judged it was old-standing. The signs were very inconstant. There had been well-marked cerebellar and pyramidal signs and cachexia, and he doubted whether the intracranial pressure was the cause of the focal signs. He thought the condition might be neuromyelitis optica; he was aware of the objections to that diagnosis, but there were equal objections to other suggested diagnoses.

Sir JAMES PURVES-STEWART said that an alternative diagnosis was that of a tumour in the posterior fossa. Some years ago he had seen a Belgian child with practically identical symptoms; in that patient the condition had come on with acute cerebellar symptoms. Later there were superadded pyramidal symptoms, sometimes on one side, sometimes on the other; there was also papillœdema, an important feature in the present case. That child had also a progressive hydrocephalus, evident in the bony cranium. On account of the acute cerebellar onset the constant papillœdema, and the signs of intermittent pressure on the pyramidal tracts, Mr. Julian Taylor had explored the posterior fossa and had found a large cystic medulloblastoma occupying the middle lobe of the cerebellum. It seemed that the occasional pressure forwards of the brain-stem against the foramen magnum was the explanation of the inconstant organic pyramidal signs. The child had died a few days later.

It was difficult to accept the diagnosis of encephalomyelitis in the present case as causing the hydrocephalus and the papillœdema. To cast further light on the case it might be useful to carry out a ventriculogram, to ascertain not only how much dilatation of the lateral ventricles was present, but also to see whether the dilatation extended to the third ventricle, the iter and the fourth ventricle. Or lipiodol ventriculograms might be carried out. Balado of Buenos Aires had shown that, with proper precautions, the injection of lipiodol into the ventricular system caused even less reaction than did the injection of air.

Dr. P. CLOAKE said that the points presented by this case were difficult to fit in with either of the suggested diagnoses. The raised spinal-fluid pressure on 9.10.34 seemed to be opposed to encephalomyelitis, as were the normal cytology and biochemistry of the spinal fluid on 13.6.34, and the progressive improvement was opposed to the idea of neoplasm. He suggested that there might be a tuberculoma. There was a tuberculous history in the mother, and the site indicated, the cerebellum, was a not infrequent site of such lesions in children.

Dr. LARKIN (in reply) said that the possibility of tuberculoma had been considered, because of the mother having had tuberculosis, but the blood-count was normal, as were the lymphocytes and leucocytes, and the Mantoux reaction was negative. There was no pyrexia when the patient got up and about, or when he was allowed out in the sun.

Myoclonia with Absent Deep Reflexes.—LEWIS R. YEALLAND, M.D.

The patient, a goods porter, aged 45, has complained of "twitches" for six years. Eighteen months ago he fell down, as the result of spasm in the legs. Since then the condition has rapidly become worse. In youth he had left otitis media and there is a large perforation of the drum and partial deafness on that side. The family history discloses no similar disability.

Physical examination.—(1) Defective convergence. The pupils react sluggishly to accommodation but actively to light. The cranial nerves are otherwise normal and the optic discs are clear. (2) Involuntary movements: Two types are observed; (*a*) fibrillary tremors in the limbs, principally to be seen over the backs of the hands and all over the thighs. When the patient's arms are extended in front of him the fingers present an irregular tremor which assumes the character of an intention tremor when he touches his nose. These slighter and more continuous spasms of the fingers materially subside when the arms are at rest, and are irregularly interrupted by severer spasms of the arms of the next type: (*b*) shock-like contractions, irregular in place, severity, and frequency, occur in the face, tongue, trunk and limbs, causing, without pain, a convulsive tic of one or other side of the face, protrusion-spasm of the tongue, lurching of the trunk, jerking of a limb or more than one limb or the two upper or two lower limbs simultaneously. He is frequently thrown to the ground and injures his left, but rarely his right, knee. Luminal favourably influences the condition. (3) Ataxy, without loss of postural sense, is present, but is slight and is more marked on the left side. There is dysarthria but no nystagmus. The gait is slightly awkward. (4) Absent deep reflexes with normal superficial reflexes. No sensory loss no wasting; and no disturbance of electrical excitability. (5) Mental state varies between depression and exaltation. Vestibular tests, cerebrospinal fluid, Wassermann test and blood-count disclose no abnormalities.

Discussion.—Dr. WORSTER-DROUGHT said that for a long time he had been hoping to see a case that could truly be described as one of "paramyoclonus multiplex" according to Friedreich's original description in 1881. The case shown by Dr. Yealland was the nearest to the description he had met with. He had seen several cases described as "paramyoclonus multiplex" in which shock-like and bilateral elevations of the shoulders occurred together with sudden extension of the arms. Most of these had been proved to be hysterical.

Paramyoclonus multiplex admittedly comprised a somewhat vague and varied group of motor disorders, and was a doubtful clinical entity. According to Friedreich's original description, the clonic contractions affected mainly the muscles of the extremities and trunk; the contractions were short and very sudden, involving a small number of muscles which did not have asynergic action. The supinator longus (radio-brachialis) was specially involved. The effect of the contractions in moving a limb was said to be absent or only very slight. On the other hand, Henoch and others had described more violent types of myoclonus, while Unverricht had recorded a familial form. The relationship to myoclonus epilepsy had also to be considered. As far as he (the speaker) was aware, no similar case had been described in which the deep reflexes were entirely absent.

Dr. MACDONALD CRITCHLEY said he had seen this condition before. At the National Hospital, ten years ago, there was a patient suffering from shock-like myoclonic twitchings of limbs and trunk. They were symmetrically distributed, and were even more marked than in the present patient. He did not remember whether the tendon reflexes were abolished. In that case the most outstanding feature had been the affection of speech, which was inspiratory in character, with a tremendous over-reaction of the muscles of expression in the face and in the neck muscles.

Sir JAMES PURVES-STEWART also remembered similar cases. He used to see a dangerous form of epidemic encephalitis, a myoclonic encephalitis, in which the abdominal muscles were specially affected, sometimes also the muscles of the shoulder-girdles. There was also "Dubini's electrical chorea," an epidemic of encephalitis many years ago in Italy.

He suggested that the myoclonus in this present case was explicable as a residuum of an encephalitic attack, and that the encephalitis had also damaged the reflex arcs so accounting for the absence of the tendon reflexes. There was, however, no available history of an encephalitic illness in this particular case. Yet it was recognized that marked post-encephalitic lesions might occur in patients with a history of mild or abortive encephalitis, or, even with no such history at all. In this case he thought the myoclonus might be a post-encephalitic syndrome.

Dr. G. S. HALL asked whether Huntingdon's chorea was a likely diagnosis.

Dr. YEALLAND (in reply) said he did not think the case was one of Huntingdon's chorea, because in that condition the reflexes were normal, and there was no fibrillation of muscles. As to Sir James Purves-Stewart's suggestion about epidemic encephalitis he (the speaker) was rather afraid it might be called that. There was certainly loss of the power of convergence in this case but in that disease one usually saw some disturbance of associated automatic movement, or lack of facial expression, features not presented in this case. It was, however, impossible to eliminate the diagnosis of post-epidemic encephalitis of ambulatory type.

He did not know whether in Dr. Critchley's case the involuntary movements were bilaterally simultaneous or not. [Dr. CRITCHLEY: Nearly so]. That did not always happen in the case presented; sometimes there was a jerk of one arm alone, at other times jerks occurred on both sides simultaneously. The abdominal muscles were involved. He thought that Dana was the first to call these cases "myoclonias," and he included under this head paramyoclonus multiplex, a term which seemed to have no meaning, as "para" meant near, and if the contraction was not in muscle where was it? In Friedreich's cases of paramyoclonus multiplex there was no alteration in the reflexes but he (the speaker) thought that the patients in those cases sometimes fell down in spasm. He believed they were much the same as the one now shown, and only differed from it in not presenting reflex changes.

Syringo-bulbo-myelia.—E. H. LARKIN, M.B.

P. R., aged 59.

History.—Sixteen years' duration. Slowly progressive until deep X-ray therapy four years ago; since then stationary.

Dissociated anæsthesia of first and second divisions of fifth nerve, without affection of third division.

On examination (7.3.24).—Dissociated hypæsthesia in the following segments:—

Right: Cervical 3, 4, 5, 6, 7, 8; dorsal 1, 2, 3, 4, 5; lumbar 2, 3, 4, 5; sacral 1, 2, 3.

Left: Cervical 3, 4, 5, 6, 7, 8; dorsal 1, 2, 3, 4, 5; complete dissociated anæsthesia cervicals *right* 3 and 4.

Reflexes: Plantar both extensor; no ankle-clonus; knee-jerks exaggerated; abdominals present.

On examination (7.7.26).—Signs unchanged, except that the right pupil was larger than the left, and the complete dissociated anæsthesia had spread to cervicals 3 and 4 on the *left*, and the left plantar was now flexor.

1929.—Signs unchanged, except that great wasting of both shoulder girdles had begun, and there was, in addition, complete dissociated anæsthesia of the upper two divisions of the right fifth nerve.

Deep X-ray therapy given to cervical spine.

1.12.34.—Pupils: Right 3 mm. Left 1·5 mm. Light, consensual, and accommodation reflexes present, both sides.

Present condition.—No nystagmus. Speech: Spastic, dysarthric.

Fifth nerve: Pain and temperature sensations absent in first and second divisions of right side. Weakness of right masseter and right pterygoids; some wasting and loss of power in sternomastoid and trapezius.

Pain-sense and thermal sense absent: Lumbar 4 to 5, right; cervical 1 to dorsal 7, right. Cervical 5 to dorsal 5, left. Vibration sense absent both arms. Deep pressure, posture, light touch, unaffected.

Reflexes: Supinator jerks equal. Biceps jerks, right present, left absent. Triceps jerks both present. Knee- and ankle-jerks both present. No ankle-clonus. Plantar reflexes, right extensor, left flexor. Abdominal reflexes present.

Great wasting of infraspinati, supraspinati, deltoids and pectorals, left latissimus dorsi and interossei of left hand. Moderate wasting of sternomastoid, trapezius and right quadriceps. Weakness of right masseter and right pterygoids.

Discussion.—Dr. WORSTER-DROUGHT said that caution was necessary in attributing apparent arrest of syringomyelia to the effect of deep X-ray therapy. It was known that syringomyeliac processes remained quiescent sometimes for very long periods. He recalled a case of his own in which the clinical manifestations were thus almost indistinguishable from those of a cervical intramedullary tumour (including increased protein content of the cerebrospinal fluid). Laminectomy had been carried out. The operation was performed nine years ago and there had since been no deterioration in the patient's condition nor any increase in the physical signs. At the same time he (the speaker) did not attribute this arrest to the laminectomy.

Dr. CLOAKE said he did not detect any weakness of jaw muscles, and that was the only sign certainly due to a lesion above the level of the spinal cord. Tongue, palate, swallowing, and speech were all unaffected, and it was probably incorrect to call such a condition syringo-bulbo-myelia; it was a myelia running into the upper part of the cord.

Dr. LARKIN (in reply) said that there was considered to be some affection of speech; rapid repetition of sounds was very poor. The response of the pterygoids and masseter on the right side to electrical stimulation was not as good as on the other side.

Left Parieto-occipital Tumour.—E. H. LARKIN, M.B.

S. M., male, aged 46. Sudden onset June 1934. "Stroke down right side."

On examination.—Signs as now present. (1) Nominal aphasia. (2) Visual aphasia. (3) Right-sided dyspraxia. (4) Right homonymous hemianopia. (5) Right sensory hemiplegia.

Operation (27.9.34).—Left temporal decompression. A tumour was found one inch from the mid-line in the parieto-occipital region; an area of brain about 1½ sq. in. seemed to be tightly stretched over a dark bluish-red mass. No attempt was made to excise it as when it was incised with a diathermy knife it bled very copiously. The condition has remained unchanged since the operation.

The movements of the right arm are the doubtful point. The arm weakness has only come on slowly, and may be due merely to the patient's not having used the arm.

Discussion.—Dr. MACDONALD CRITCHLEY said that one point calling for comment was the right-sided dyspraxia. Surely with a lesion in this particular location he must have had a bilateral apraxia. Certainly this evening he had all the marks of a left-sided apraxia as well. He would like to have the opinion of Dr. Maas.

Dr. OTTO MAAS said that in the case which he had originally described in association with Dr. Liepmann, testing could not be carried out on the right side because there was hemiplegia, but on the left side there was apraxia.

Dr. LARKIN (in reply) said that several consultants had seen the patient before the operation, and they thought there was no impairment of motor function on the left side; the patient could coördinate movements with the fingers very well. He was having deep X-ray therapy to the tumour. For the last four days signs had been developing which had not been present before. The right plantar reflex was now doubtful, and the patient was more awkward with the left arm than previously. Only that day inequality of the pupils had developed.

Dystrophia Myotonia associated with Hemi-analgesia.—OTTO MAAS, M.D., and MACDONALD CRITCHLEY, M.D.

P. P., male, aged 30, patient of St. Andrew's Hospital, Bow, complains of general debility for two years, together with weakness of the grips.

Family history.—Mother died at age of 62 from pneumonia; during life she "had some similar trouble in the hands." One brother alive and well. No evidence of cataract in the family.

On examination.—Weakness and wasting of the facial and mandibular muscles. Wasting of sternomastoids and of the small muscles of the right hand. Mechanical myotonia demonstrable in tongue and thenar eminences and in calf-muscles. Difficulty in relaxing hand-grasps. No obvious sign of cataract, but slit-lamp examination has not yet been made. Speech typically affected. Right-sided impairment of pain-sense and temperature-sense. Reflexes normal. On flexor aspects of both forearms are one or two small subcutaneous ? fibromata.

Discussion.—Dr. OTTO MAAS: I think the diagnosis is settled. One sees the myotonic reaction when the patient is asked to stretch his fingers and there is a myotonic reaction when one taps the thumbs and the tongue. There is wasting of both sternomastoids and of the small muscles of the left hand. The right brachio-radialis muscle is wasted; the left one is well-preserved and has good function. There are signs of affection of the spinal cord. In opposition to what I have written in the notes there is a definite dorsal Babinski on the left side. Right-sided impairment of pain-sense and temperature-sense. The tuning-fork is better felt on the right side of the body, the face and the limbs. The eye-examination which was carried out at St. Andrew's Hospital revealed no cataract. A good description of such a case was published by Rindfleisch (*Deutsche Zeitschr. f. Neurenheilk.*, Band 33) in 1907. We know that syringomyelia is a hereditary disease like myotonia.

Dr. YEALLAND said that the loss of sensation was on the same side of the face as on the trunk. Moreover, the corneal reflex was normal on that side. He asked whether the hemi-anæsthesia was not functional in type. It seemed impossible to attribute this loss of sensation to syringomyelia; if so, where was the lesion?

Dr. WORSTER-DROUGHT said that the interesting feature of this case was the hemi-analgesia which certainly appeared to be organic in type. So far as he was aware this did not occur in connexion with dystrophia myotonica and could only be accounted for by the existence of a concurrent syringomyelia. Was this suggested?

Dr. MAAS (in reply) said the fact that there was a definite dorsal plantar reflex proved that it was an organic affection of the central nervous system. He thought also the fact that the sensibility to touch was preserved, in opposition to the sensibility to pain, was in favour of the organic nature of the condition. By the kindness of Dr. George Riddoch he was examining a family in which were many cases with definite symptoms of myotonia atrophica. One youth, aged 20, was excellent at boxing, football, tennis, etc., and yet had definite symptoms of myotonia atrophica.

[*The report of other cases shown at this Meeting will be published in the next issue of the* PROCEEDINGS *of the Section.*]

Section of Ophthalmology

President—RANSOM PICKARD, C.B., M.S.

[*January* 11, 1935]

Corneal Graft.—B. W. RYCROFT, F.R.C.S.

Mrs. E. W., aged 48, attended the Royal Eye Hospital, July 1920, under the care of Mr. Dorrell.

Diagnosis.—Right eye: Tuberculous keratitis of two years' duration; vision = perception of light. Left eye: old corneal nebulæ; vision $\frac{6}{18}$. Wassermann reaction faintly positive. Treatment by tuberculin injections and the usual local remedies. Ceased attendance 1922.

October 1923: Attended hospital again, under the care of Mr. Letchworth. Relapse of left eye keratitis; continuation of tuberculin injections. Corrected vision (left) = $\frac{6}{18}$.

December 1924: Right eye enucleated on account of secondary glaucoma. January 1925: Superficial keratitis (left) treated. April 1930. Acute kerato-iritis (left).

January 1931: Left vision $\frac{6}{60}$. General investigations. The Wassermann was negative; urine analysis negative. Dr. Oddy reported that no active tuberculosis had been detected on either clinical or radiological examination.

October 1933: Left vision: perception of light. Commencing staphyloma of cornea.

June 1934: Referred for local ultra-violet radiation. There was accurate projection but no perception of hand movements. It was impossible to discern the pattern of the iris either by diaphanoscopy or by direct slit-lamp examination; the pupil could not be seen.

November 1934: Complete investigation was carried out, with negative results, apart from an increase in the blood-sedimentation rate.

December 4, 1934: *Operation.*—Under cocaine anæsthesia, seventh nerve-block (O'Brien). 4 mm. corneal graft, conjunctival flap; continuous saline irrigation. No corneal sutures.

December 28, 1934: L.V., with $\frac{-1}{-1}$ axis 180°, = $\frac{2}{60}$.

January 1, 1935: L.V., $\frac{-1}{-1} = \frac{4}{60}$ J.15.

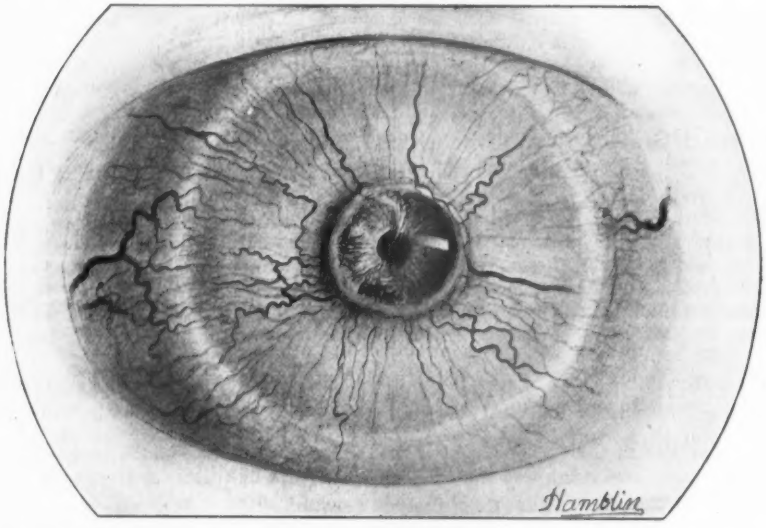
January 4: L.V. = $\frac{6}{60}$ J.14.

January 7: L.V. = $\frac{6}{24}$ J.4 with telescopic correction.

This is a case of corneal grafting, by a technique which is not original; the object was to see if the technique in vogue could be simplified. We had at the hospital a donor who came in on account of copper wire having been driven through the upper eyelid, causing a series of recurrences of hæmorrhage in the vitreous, and general irritability of the eye. Eventually the eye was removed, and we were able to use the cornea. Preliminary sterilization by ultra-violet-light irradiation was carried out.

The graft was the same size in host and donor, and I tried to shelve the graft in both cases, on Mr. Tudor Thomas's recommendation. Members can see that the iris is fixed, and that this coincides with the pupillary aperture.

On the third day the graft could just be seen through the aperture; it was completely opaque, and looked like soft blotting paper. Seven days later it was clear, the stitch had cut out, and the conjunctiva began sliding back.



A week ago vision was $\frac{6}{18}$, and with telescopic spectacles $\frac{6}{24}$, and J.4 for reading.

Mr. TUDOR THOMAS congratulated Mr. Rycroft on the result achieved in this case. The graft had a clear shining surface, and the vision ($\frac{6}{24}$) was very gratifying.

Mr. Rycroft had mentioned the difficulty in deciding the position of the pupil. This could be determined by transillumination if two transilluminators were used, and by observing the lighted patch on the cornea one was able to estimate the depth of the anterior chamber and the position of the pupil, and could arrange the graft to coincide. In dealing with a small pupil, particularly with a small fixed pupil, it was important to have the graft immediately in front of it. He (the speaker) had had one case—a good one—in which the graft was reasonably clear, but it did not quite correspond with the position of the pupil. That was one of his earlier cases, and he had not localized the pupil with sufficient exactitude. It was a case of old superficial keratitis, and the pupil was bound down to the lens. In an attempt to give the patient better vision he had tried to perform iridectomy in order to enlarge the pupil downwards, but the iris tissues were so tough and fibrous that it could not be done. Some time later he had tried again, and this time had succeeded in enlarging the pupil or pulling it downwards. Meantime, however, the trauma to the eye had done considerable harm to the graft, which became practically opaque. The lesson to be learned was, that a graft which was clear should be, as far as possible, left alone; and that it was important to take every possible precaution before commencing operative treatment to get everything right with the utmost precision. Where an iridectomy had been performed, or in cases in which the pupil could be fairly easily dilated with atropine—and that could be found out by transillumination—the importance of the position of the graft was not so marked.

He (the speaker) had not, as yet, published a detailed account of the technique he followed in carrying out corneal grafting in human beings.

His results had been as follows: Out of 15 cases 10 were, he considered, successful, the criterion of success being that there was a retention of a certain amount of clarity, and a decided usefulness of vision. The patient, whom he had shown at the last ordinary meeting of the Section, and in whose case the operation had been successful, had, unfortunately,

died not long after the meeting. He was subject to high blood-pressure, and had acute nephritis, from which he died on the eve of his departure for his home in New Zealand. His vision had become $\frac{6}{60}$.

He (Mr. Tudor Thomas) was much pleased to see this case of Mr. Rycroft's. He thought that in a few years, when ophthalmic surgeons had carefully compared their technique and experiences, it would be possible to put the subject of transplantation of the cornea on to a proper basis, and thus give a large measure of hope to sufferers from corneal opacity.

Two Brothers, members of a family with "lobster-claw" (split-hand and split-foot deformity), one showing the Skeletal Deformity and the other Aniridia.—L. H. SAVIN, F.R.C.S., and ARNOLD SORSBY, F.R.C.S.

The history of this family was recorded in 1908 by Sir Thomas Lewis and Dr. Embleton (*Biometrica*, 1908-9, vi, 26). The patients are the only children of an affected father.

Edward G., aged 23, shows the skeletal defect. His eyes are normal.

Herbert G., aged 20 is blind. He came under observation at the Royal Eye Hospital at the age of 5 ; aniridia and congenital subluxation of the lenses were noted. At the age of 6, vision was $\frac{6}{6}$ in each eye. Owing to recurrent attacks of inflammation the right eye is now completely shrunken. The left lens has become partially opaque. This patient's hands and feet are normal. No evidence of ocular abnormalities in other members of this family.

These cases are shown to bring out the linking up of skeletal defects with eye defects. The following is a list of some recognized associations :—

Familial Digital Abnormalities in Relation to Eye Defects.

(1) Syndactyly associated with aniridia.
(2) Arachnodactyly associated with congenital subluxation of lenses.
(3) Polydactyly associated with retinitis pigmentosa—probably incompletely described cases of
(4) Laurence-Moon-Biedl Syndrome.
(5) Brachydactyly associated with microcornea.
(6) Doubling of thumbs with atrophy of terminal phalanges (apical dystrophy of hands and feet) associated with bilateral macular coloboma.

Exudative Retinitis.—HAROLD RIDLEY, F.R.C.S. (for HUMPHREY NEAME, F.R.C.S.)

Sylvia D., aged 8 years.

Mother noticed that since the age of 4 years the child's right eye shone in certain lights ; she is uncertain as to whether the child has ever seen with the eye. Five older children all healthy. Mother's brother had eye removed at the age of 6 years on account of "decay." Grandmother was Maltese, which probably accounts for the pigmentation.

On examination.—Right eye : Vision, perception of light. No injection ; cornea bright ; no k.p. ; pupil active ; faint vitreous haze with cells in retro-lental space. Fundus : optic disc normal ; large yellowish-white mass in macular area deep to retinal vessels, raised 3 d.d. above retinal level. Another similar but larger patch between macular and temporal periphery raised 7 d.d. ; retinal vessels in this area show dilatation and tortuosity ; numerous small retinal hæmorrhages and two dark areas on surface of mass—probably absorbing hæmorrhages. The vessels generally are somewhat tortuous and a few small branches in the normal area show dilatation. No serous detachment. Many small glistening patches of subretinal exudate between the two masses.

Left eye : Vision $\frac{6}{6}$. No abnormality found.

General examination.—No abnormality found. Reports of Wassermann and Von Pirquet reactions not yet issued.

Two Cases (Brother and Sister) of Familial Macular Degeneration in Adolescence.—HUMPHREY NEAME, F.R.C.S.

This condition is not common. The fundus appearance is different in the two cases. The sister has somewhat massive blotches of pigment in the macular area, while in the brother the appearance is more granular or "peppery."

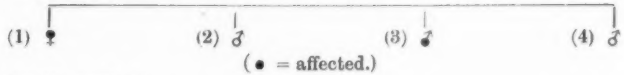
The boy, Norman K., aged 11 years, in April, 1934, had

R.V. with $\frac{-\ 0{\cdot}75}{+\ 0{\cdot}75\ /\ 70°} = \frac{6}{12}$ (partly); L.V. with $\frac{-\ 0{\cdot}75}{+\ 0{\cdot}75\ \backslash\ 110°} = \frac{6}{9}$ (partly).

On January 5, 1935, the vision was reduced, with the glass, to $\frac{6}{24}$ in each eye. The eyes were examined under atropine, and a slight alteration in the correction made no improvement. Both maculæ showed finely stippled pigmentation over an area nearly equal to that of the optic disc. The change is more marked in the centre of each area.

Beatrice K., aged 24, was, according to her mother, a patient at Moorfields Eye Hospital some years ago, at about the same age as that of her brother at present—that is to say, 11 years. Each macula shows several dense, roughly circular patches of black pigment, of sizes up to about one-fifth of the disc diameter, with a few smaller spots around. In the right, there is also a delicate pigment ring, probably bordering the fovea. She is unable to read ordinary print.

Family history—



(● = affected.)

(1) Beatrice K., aged 24.

(2) A brother, aged 21. Alive and well. Sight good without glasses. Occupation, plumber-jointer in electrical trade.

(3) Norman K., aged 11.

(4) A brother, died nine and a half years ago, aged 9 months, of meningitis.

No history of eye defect in previous generation obtained.

Choroidal Sclerosis

By ARNOLD SORSBY, F.R.C.S.

(*Abstract*)

THE reported cases in the literature on choroidal sclerosis fall into three more or less distinct groups.

(1) "Central senile areolar choroidal atrophy" described by Nettleship in 1884. This is shown as a relatively sharply circumscribed oval area extending from the disc to well beyond the macula, revealing varying degrees of atrophy of the choroidal vessels. The condition is bilateral.

(2) Massive peripapillary choroidal sclerosis. An illustration of this condition appears in Haab's Atlas. The lesion manifests itself as a coronary radiation from the disc; choroidal vessels in varying degree of obliteration are seen.

(3) Generalized choroidal sclerosis. An illustration of this condition was given by Stanford Morton in 1885 under the name of atrophy of the choroid. There is a generalized obliteration of the choroidal vessels.

In all these conditions a varying degree of pigmentary disturbance was present and subsequent cases have brought out old age, syphilis, and a possible familial incidence, as ætiological factors. None of these however are conclusive, as cases in young people have been reported and syphilis was absent in all but three cases described.

The possibility of a familial factor is based on the inconclusive cases of Cuperus, Guglianetti and Wilmer, none of whom, however, has actually seen familial cases, though the histories they give are suggestive. The cases now shown bring out two factors of interest. Two cases of "central senile areolar choroidal atrophy" in brothers with a history of failing vision since the age of 20 are shown; a brother and sister showing generalized choroidal sclerosis, with a history of failing vision since childhood are also demonstrated. Three further cases without familial history are shown. Three of these seven cases show marked cardiovascular disturbances.

One of the problems raised is whether it may not be possible to distinguish two types of retinitis pigmentosa, one being a primary retinal dystrophy and the other a retinal degeneration secondary to choroidal obliteration. The rôle of choroidal sclerosis in macular disturbances occurring in old people is another consideration. One final point is the diagnosis of sclerosis, as distinct from obliteration, of the chloroidal vessels in the conditions generally passing under the name of choroidal sclerosis.

Illustrative Cases

Central Senile Areolar Choroidal Atrophy (Nettleship) in Two Brothers.—ARNOLD SORSBY, F.R.C.S.

(1) George R., aged 63. General condition good (Dr. G. Konstam). Irregular extension peripherally of the central sclerosis.

(2) Richard R., aged 59.

The family history is negative. Parents not consanguineous. Vision in both these patients has been failing since the age of 20. No nightblindness.

Massive Peripapillary Sclerosis.—ARNOLD SORSBY, F.R.C.S.

Walter S., aged 60. Sight failing for ten years. No nightblindness. General investigations (Dr. E. J. R. Leiper) negative.

Generalized Choroidal Sclerosis in a Brother and Sister.—ARNOLD SORSBY, F.R.C.S.

Thomas S., aged 60.

Mrs. R. L., aged 62.

Vision failing since childhood. No definite nightblindness. A younger brother, now dead, was blind. Family history otherwise negative.

Choroidal Sclerosis.—ARNOLD SORSBY, F.R.C.S.

G. W., male, aged 77. Sight has been failing for two or three years.

Choroidal sclerosis shown by exaggerated fundus tigré and a few white vessels. In the right macular area is a deep-seated, raised white mass, ? organized choroidal hæmorrhage. Left macular area: loss of foveal reflex with uniform mottling. General investigation (Dr. T. J. Kelleher and Dr. K. May) negative, except for some calcification of vessels of legs.

Generalized Sclerosis without Family History.—ARNOLD SORSBY, F.R.C.S.

(7) Frederick Y., aged 67. Iridectomy in each eye in 1903, in America. Posterior synechia in right eye: B.P. 220/140. Systemic vessels—generalized sclerosis. Numerous extra-systoles. (Dr. V. Wiley.)

Discussion.—The PRESIDENT said he was not so entirely convinced as Mr. Sorsby appeared to be of a distinction between some cases of retinitis pigmentosa and those now described. He (the speaker) remembered many cases of retinitis pigmentosa which, in the final stage, had shown sclerosis of the choroid, but had not shown it in the early stage. On the other hand, he had seen advanced cases with much apparent sclerosis of choroid but in which the pigment was so typical that no one would refuse to believe that there was at least an element of retinitis pigmentosa in it.

He would like to know whether anything had been done on the question of the visual fields in the more limited cases. In the advanced cases one could get nothing, but he had wondered if anything could be done with regard to the fields, especially fields for colour. His view was that the field for blue was especially affected in choroidal cases, and it might be possible to trace the progress of the condition early, and fairly accurately, by some such means.

Mr. EUGENE WOLFF said that if such microscopic sections from these cases of choroidal sclerosis were examined it would probably be found that there was obliteration of the choriocapillaris; this seemed to be the only way in which one could explain the appearance of the fundus. The retinal pigment epithelium, nourished by the choriocapillaris, had, in parts, disappeared (this was why the choroidal vessels were so clearly seen), and the degenerated pigment had invaded the retina. That, he thought, must depend on obliteration of the choriocapillaris.

Mr. SORSBY (in reply) said that the question of retinitis pigmentosa was a difficult one, and the subject was too large to be properly dealt with in an incidental discussion.

With regard to the fields: All the patients with generalized choroidal sclerosis had also a reduction of vision to such a degree that they had no more than perception of light, or, at most, ability to count hand-movements, and for that reason there had been in these cases, no question of taking the visual fields. It was to be hoped that earlier cases would be met with, and it was possible that in such cases interesting results would be obtained, but he was not hopeful of such a line of approach. A restricted field might be due to a primary degeneration of the retina or to death of the retina from an unsatisfactory underlying choroidal circulation. Differentiation of the types of retinitis pigmentosa was, he thought, more likely to be accomplished by a study of the genetic behaviour and the type of general complications, perhaps ectodermal in the retinal variety and mesodermal in the choroidal.

Mr. Wolff's remark as to the obliteration of the choriocapillaris raised another difficult problem, namely, as to what happened when one saw, clinically, the disappearance of the choriocapillaris and occlusion of the larger choroidal vessels. Sometimes it was possible to see sclerosis affecting the small vessels, and the network of these vessels stood out well; in other cases there was no evidence of choriocapillaris, but there was sclerosis and obliteration of large vessels. Whether the choriocapillaris died first, and as a result, the overlying retinal pigment died and became scattered, allowing the choroidal circulation to become visible, he did not know. It was possible to argue a case for the primary change being in the retina with the subsequent changes showing themselves in a closing down of the network of vessels which were no longer needed.

[*An account of the Depth-Perception Exerciser shown by the President will be published in the next issue of the* PROCEEDINGS *of the Section.*]

Section of Otology

President—E. A. PETERS, F.R.C.S.

[*December* 7, 1934]

DISCUSSION ON MENINGITIS OF OTITIC ORIGIN

Mr. T. B. Layton: I propose to describe otitic meningitis in three stages; but shall first make some preliminary remarks upon: (*a*) The limitation of my subject. (*b*) Lumbar puncture. (*c*) Treatment that is common to all stages.

(*a*) Clinically cases of otitic meningitis fall into two groups: (1) Those which arise from the newly infected mastoid, and (2) those which arise in the presence of old disease.

I propose to refer only to the former, and to exclude extension of inflammation to the brain.

(*b*) I divide lumbar puncture into: (1) Diagnostic; (2) prognostic; (3) therapeutic.

(1) By *diagnostic* lumbar puncture I mean one which is performed to distinguish an otitic from other forms of meningitis. By it we gain help to determine the presence of tuberculous or cerebrospinal meningitis in a patient suffering from an otitis media when the case does not present the usual symptomatology.

(2) By *prognostic* lumbar puncture I mean one which is performed to tell the stage to which the disease has progressed. By it we gain help to determine whether the routine treatment common to all cases is sufficient, or whether this need be supplemented by some other therapy.

(3) *Therapeutic* lumbar puncture may be classified thus: (i) Drainage of the theca, which may be intermittent or continuous. (ii) Insertion into the theca of drugs and sera.

(*c*) The essential treatment in every case of otitic meningitis is to remove the factory of organisms in the mastoid or other part of the temporal bone which is in contact with the dura mater. If this be done no case is hopeless. If it be not accomplished the chance of recovery is negligible even in the earliest case.

The treatment that the medical officers of the fever hospitals of London have helped me to work out, and that is now the routine at those hospitals where I attend, is as follows:—

The mastoid is opened, and if a track of disease can be recognized leading down to the dura mater, it is followed, and the bone in contact with this is removed widely around the area of contact. If no such track can be recognized, the bone is removed widely from both middle and posterior fossæ. Steps are then taken to fix the wound widely open. To do this the margin of the pinna should be sewn to the skin of the temporal region. It cannot be too strongly emphasized that the ordinary mastoid wound when left, even if packed with gauze, remains a closed one, with no more than 15° between the two walls. By sewing the pinna forward the angle approaches 180°.

The cavity is then hosed with saline, using anything up to a couple of gallons. The container is held high, and the nozzle at some distance from the wound, so that a good

stream plays upon it to remove every scrap of bone, of pus, of granulations or of blood-clot. It is then lightly packed.

In the after-treatment I lay most stress upon large quantities of fluid. The patient must be propped on pillows, with the head sideways, so that no movement of the neck is needed when he drinks or takes food. The fluid must be kept ready by the bed-side, so that anyone coming to see him can put the feeding-cup to the lips and coax him to take an ounce or two. In this way 300 oz. (2½ gallons) have been taken by an adult. For a child of six the minimum is 120 oz. (¾ gallon). The amount should be lessened as soon as the patient has turned the corner.

Secondly I give solid food at once. Thin bread and butter can be given in less than twelve hours from the operation, and other things added during the day. The benefit is seen on the second or third day, for it is always an effort for a patient to start taking solid food, and he may thus be taking a quantity of nourishment at a time when otherwise he would be trying to start. The early administration of solid food is also a valuable guide to the progress of the patient; the refusal to take it on the second or third day after having done so on the first may be the earliest sign of there being something needing further operative treatment or some accessory therapy.

For two, three, or even four days after the operation, the wound is dressed and the hosing is repeated twice or thrice daily, according to the condition of the patient and the progress of the disease. Absolute rest is essential at all other times. No visitors should be allowed, and it is well if the room can be darkened. By the end of the fourth day, and probably of the third, the patient is well on the way to recovery, or is going downhill and the case is hopeless.

With these preliminary remarks I pass on to the description of otitic meningitis in three stages.

(*A*) *The early stage.*—The symptoms of otitic meningitis are bilateral and proceed from above downwards. The first is a rigidity of the neck. The first stage then is that at which this alone is present. The symptom is absolutely characteristic and should be elicited thus:—

Take the pillows away so that the patient lies flat on the back; put the two hands as you face him behind his head so that the thumb and three fingers of each hand are behind the occiput while the little fingers lie against the muscles of the neck. Then get the patient to leave the movements of the head in your hands, and bend the head towards the chest. If he can put the chin freely down on to the sternum he has not got meningitis. If, however, he cannot do this he almost certainly has, and the suspicion is confirmed by two other points. First, the character of the pull of the muscles. It is the sensation one gets when pulling longitudinally on a wet piece of string. Second, the feel to the little fingers of the complexus muscles. These stand out rigidly under the trapezius and cannot be pushed in by the finger.

As soon as this symptom is present the treatment outlined above should be instituted. Recovery ought to ensue. Every hour, however, that is lost endangers the patient's life. Lumbar puncture should not be done. It results in delay. It hurts and distresses the patient unnecessarily. It tells you nothing that you do not know already. The fluid will be under some increase of pressure, it will be unaltered in naked-eye appearance, the chemical and cytological examination will not show sufficient change to tell more than you know from the neck rigidity and the report on it will arrive too late to be of use. Lastly by disturbing the intrathecal circulation it may do harm.

There are those who say that this stage is not one of meningitis. I do not mind what you call it so long as you get busy. But do not call it *meningism*. This word by origin, by tradition, and by its very sound, is associated with inactivity. I find by experience that practice is usually based upon an association of ideas and in this you need a term that infers immediate and vigorous business. If you refuse to call this stage meningitis, call it *meningeal irritation*, and as you roll it off your tongue it will spur you to activity and will help you to sweep away all those

suggestions for delay that come from parents, doctors, nurses, and from yourself, urging that the operation should be done to-morrow instead of to-day.

(*B*) *The second stage.*—Where rigidity of the neck alone is present the great majority of patients should recover.

The second stage is that in which Kernig's sign is present in addition to rigidity of the neck.

The state in which Kernig's sign is not present, but you cannot be sure of its absence, forms the boundary zone between the first and second stages of otitic meningitis.

The similar boundary zone between the second and third stages is that state in which the abdominal reflexes are lost with or without the presence of headache.

Headache is due to distension of the theca with fluid. I have not found it an early symptom and would class it in the late secondary stage.

Neck rigidity and Kernig's sign are the only symptoms of otitic meningitis of clinical importance. To save the patient's life you must act before anything else develops.

In this second stage a prognostic lumbar puncture should be done either when the patient is under the anæsthetic before the operation or on the next day at the time of the first dressing. Which occasion is chosen will depend upon the time at which the operation is done and the accessibility of the laboratory, for the report upon the fluid is vitiated unless the examination be made within an hour or two.

If the fluid in the manometer is clear and the pressure not high nothing more need be done. If clear, but under an increase of pressure, sufficient should be removed to reduce it to normal; but if cloudy more should be drawn off, the exact amount depending upon whether the patient is under an anæsthetic or not.

If the fluid is clear the treatment should be that described for the first stage, but if it be opalescent this should be supplemented by lumbar puncture twice or thrice daily for several days. This should be performed sufficiently often and freely to relieve headaches and rigidity of the back.

(*C*) *The late stage.*—In this the patient lies on his side with the knees bent up, the back extended and the head thrown back. A cry escapes him from time to time owing to the severity of the headache. The lips are parted, the mouth is dry, the tongue is heavily furred and the temperature steadily mounting; but it is characteristic of the condition that the symptoms are exactly bilateral.

A prognostic lumbar puncture must be done. In the examination of the fluid I lay most stress upon two observations, the number of cells as indicated by the degree of opacity, and the presence of organisms.

With regard to the latter, a clear distinction must be made between these cases in which a hæmolytic streptococcus can be grown *in vitro* and those where an organism, probably the hæmolytic streptococcus, can be observed by direct observation in a smear. The former is of pathological interest only, it is of no clinical value. The fight is over before the report arrives.

Intermittent thecal drainage is, I believe, still our stand-by for the milder cases of this group, where the symptoms are not as yet very severe, where the fluid is not opalescent, and where no organisms can be detected under direct observation.

The insertion of any antiseptic drug is, I believe, valueless.

When organisms are seen by direct observation in a smear I used to think the case absolutely hopeless. Is this so? or will a case occasionally recover? It is the possibility of this occasional recovery which must stimulate us to ponder on what we should do.

The treatment common to all cases is not enough. Whether the addition of intermittent thecal drainage will occasionally save a case I do not know. It is not

to be relied on. What more must we consider? Every British otologist of our generation owes a debt of gratitude to Mr. G. J. Jenkins for his perseverance and devotion to duty in dealing with otitic meningitis, and yet I believe his work has lain chiefly with clinical types different from those I have been dealing with to-day. I do not think his operation of translabyrinthine drainage is applicable to these cases except where the access of the disease to the meninges was across the labyrinth.

It seems that the time is ripe for two other lines of treatment to be attempted. The one is to take a leaf from the book of the physicians and to add to intermittent drainage of the theca the replacement by a serum either of a specific or of a non-specific nature, and the other is to replace intermittent by continuous thecal drainage.

It is along one of these lines that each of us must work in the future, but I urge that the first thing to do is clearly to define the type of otitic meningitis in each case that is recorded.

Mr. Norman Jory: The cerebrospinal fluid is of great interest to otologists in the various intracranial complications of aural disease.

Normal cerebrospinal fluid.—Before proceeding to consider the fluid in pathological conditions, it would be well briefly to enumerate the more important characteristics of the normal.

Pressure: The normal pressure, with the patient horizontal and relaxed, is between 100 and 200 mm. water. Greenfield advises that the pressure should always be taken before any fluid is withdrawn by puncture, and that it is unwise to continue withdrawal after the pressure has fallen to two-thirds of the initial value.

Massermann (1934) finds that after the removal of from 10 to 20 c.c. the fluid re-forms at the rate of about 0·3 c.c. per minute, while in pathological conditions Levinson (1929) found as much as 1 litre produced in twenty-four hours.

The normal fluid contains all the inorganic ions present in blood-plasma, as well as readily diffusible organic substances such as glucose, urea, uric acid, lactic acid, amino-acids and creatinine. Chlorides and magnesium are in much greater amount than in plasma; calcium, potassium, inorganic phosphorus, creatinine, amino-acids, uric acid and sugar in much less.

Cytology: The fluid arising within the ventricles from the choroid plexuses is devoid of cells, but as it passes through the ventricles, the iter of Sylvius, and down the spinal canal it acquires from one to five cells per c.mm. from the surface of brain and meninges with which it has been in contact.

The mechanism of production of the fluid is still not known with certainty.

Fremont-Smith (1933) has considered the arguments for and against the theories of secretion and dialysis, and comes to the conclusion that while, on the whole, the dialysis theory is the more probable, yet it cannot be assumed to be the whole truth in the present state of our knowledge.

The fluid in pathological conditions.—Under pathological conditions the characters of the cerebrospinal fluid are altered, and these alterations may be helpful in diagnosis and prognosis.

Pressure: Pressures above 200 mm. are definitely pathological. Any factor tending to raise the intracranial venous pressure will raise the capillary pressure in the choroid plexus, and result in increased fluid formation. The same mechanism will delay absorption. A practical application of this principle is the Queckenstedt-Tobey-Ayer test for occlusion of a lateral sinus.

In meningitis several factors operate to raise the tension, mainly cerebral vasodilatation, and obstruction to absorption due to exudate blocking the circulation of the fluid, and blocking the Pacchionian bodies.

Cytology: An increase in cell-count up to six or ten per c.mm. is suspicious, and over ten definitely pathological. The cells found are mainly derived from the blood-stream—polymorphonuclears, lymphocytes, and mononuclears. The total count usually ranges between 5 and 500 in cases of so-called aseptic meningitis, and between 1,000 and 10,000 in cases of acute septic meningitis.

It should be remembered, as Greenfield points out, that a leucocytosis in the C.S.F. may be found with a degenerating glioma of the brain, very similar to that associated with cerebral abscess. As a general rule, however, a high polymorphonuclear count indicates a bacterial infection of the meninges or central nervous system.

Chemistry: (1) *Protein*, mainly albumin, shows varying increase. A total of over 45 mgm. % is considered abnormal, and it may rise to 1,000 mgm. %; but its amount appears to give no guide to the prognosis of an individual case.

(2) *Chlorides*: The normal content, expressed as NaCl, varies from 710 to 745 mgm. %, average about 725, whereas normal plasma chloride varies from 570 to 620 mgm. %, average 595. Mestrezat (1912) was one of the first to note that the chloride concentration of the C.S.F. was higher than that of serum, and he further reported its decrease in meningitis, epecially in the tuberculous variety. Greenfield, studying cases of meningitis following head wounds, found that in seven fatal cases the chlorides fell to under 680 mgm. before death, while in one case in which the patient recovered, although pus and Gram-negative diplococci were present in the C.S.F., the chlorides remained at the normal level. He supposed, with Mestrezat, that the fall in C.S.F. chlorides was due to increased permeability of the meningeal blood-vessels. Linder and Carmichael have shown, however, that there was a coincident fall in the plasma chlorides.

Four cases of meningitis were investigated at St. Bartholomew's Hospital, two tuberculous, one chronic meningococcal and one streptococcal.

Taking the usually accepted ratio $\frac{\text{Cl plasma}}{\text{Cl C.S.F.}}$ as 0·895

In the tuberculous cases ratio was 0·86 and 0·90
In the chronic meningococcal cases ratio was 0·87
In the streptococcal cases ratio was ... 0·90

Greenfield and Carmichael point out that after exposure of the dura mater by operation, especially in the posterior fossa, the chloride content of the C.S.F. varies enormously for two or three weeks. This would explain apparent anomalies in the rule laid down by Greenfield that a low chloride content presupposed a generalized meningitis, and so carried with it the gravest prognosis.

(3) *Glucose*: The normal relationship of 45-65% of blood-sugar remains fairly constant in disease, except in meningitis. Here the reduction is due to glycolytic ferments liberated by dead cells or bacteria, and is progressive after the fluid has been withdrawn from the body. In aseptic purulent fluids the amount of glucose varies within wide limits, depending apparently on the number of polymorphs which have been killed. It is evident that the glucose content *per se* is not so important as the chlorides as a diagnostic and prognostic aid. All we can say is that in generalized septic meningitis glucose is reduced or absent, and that in aseptic meningeal reactions to intracranial septic foci it is usually normal, unless large numbers of dead polymorphs are present, when it is reduced in varying amounts.

(4) *Magnesium* has been extensively studied by McCance and Watchorn (1932) in a series of cases of meningitis, tuberculous and pyogenic, and their results they have summarized thus: In chronic meningitis, tuberculous or pneumococcal, subnormal amounts of magnesium have been found in the C.S.F. A fall has not, however, been observed in the acute cases. The fall has been found roughly to run

parallel with the well-known fall in chlorides. In one chronic case in which the patient recovered the C.S.F. magnesium returned to normal.

Other constituents of the C.S.F. have been the subject of extensive study, but are of little practical interest to otologists.

Bacteriology.—The organisms most commonly isolated from otogenous cases of meningitis are streptococci, pneumococci, staphylococci, and the influenza bacillus.

Naturally the growth of organisms from the C.S.F. implies the gravest prognosis, though the converse does not always hold, as it is a common experience to meet cases with sterile fluid proving fatal, and showing at autopsy purulent meningitis.

I have been able, by the courtesy of Mr. Sydney Scott, to investigate thirty-nine cases of acute septic leptomeningitis occurring in the Aural Department of St. Bartholomew's Hospital during the past ten years. Thirty-six cases proved fatal; in three recovery took place. Of the latter, two had streptococci in the cerebrospinal fluid, the other presented clinical, but no bacteriological, proof of meningitis. In fairness it should be realized that many of these patients when first seen were moribund with the disease; in some the condition was so desperate that any operation was frankly hopeless, in others an operation was performed in the hope that it might effect a miraculous recovery, such as is recorded from time to time in the literature. In the 36 fatal cases the sexes were equally represented. The great majority were in children; 18 cases being 10 years of age or under, 5 cases 20 years or under, 4 cases 30 years or under, 0 cases 40 years or under, 2 cases 50 or under, 4 cases 60 or under, 2 cases 70 or under, 1 case under 80. In nine of these cases (quarter of the total), the otitis media was chronic, and as might be expected these comprised the older patients, average age 38, youngest 4, oldest 74. Four cases were subacute, youngest 5, oldest 64, average 30. In the remaining 23 cases the otitis media was acute. The mastoid was the seat of acute or subacute inflammation in 29 cases, including one case with cholesteatoma formation; and of chronic inflammation in 3 cases, including one of cholesteatoma, and one on which a radical mastoid operation had previously been performed.

In the remaining 4 cases the mastoid condition was not ascertained either ante or post mortem.

Micro-organisms were recovered from the cerebrospinal fluid by lumbar puncture in 21 cases. They comprised streptococci in 11 cases, of which 5 were hæmolytic; pneumococci in 9 cases, including 1 associated with *B. Pfeiffer*, one type III and one thought to be type III; and hæmolytic *Staphylococcus aureus* in one case. In two cases no examination of the C.S.F. was made, but in one of these the diagnosis was confirmed at autopsy. In the remaining 13 cases the C.S.F. from lumbar puncture proved sterile, and no organisms were seen in stained films. In eight of these cases an autopsy was secured, and in each confirmed the diagnosis made during life.

Treatment.—The appropriate mastoid operation was performed in 31 cases, Schwartze's operation in 26, radical mastoid in 4, and Küster's operation in 1.

Lumbar puncture was done in all cases, and repeated, where possible, once or twice daily—in one case on 17 occasions.

One pneumococcal case and two streptococcal cases were treated with the appropriate antiserum, given intrathecally by the lumbar route. One other streptococcal case was treated by combined cistern and lumbar puncture, spinal wash-out and introduction of scarlet-fever antitoxin. In six cases thrombosis of the lateral sinus was present, and in one of these cases there was in addition cavernous sinus and in another multiple sinus thrombosis. In all these cases the lateral sinus was obliterated, clot evacuated, and the internal jugular vein ligatured. In one further case thrombosis occurred, and was treated as above, ten days after the primary operation. One case presented signs of acute labyrinthitis, and a superior vestibulotomy was performed.

Translabyrinthine drainage was resorted to in two cases only. In three cases an abscess of the temporosphenoidal lobe was drained, in one case the cerebellum, and in another the temporosphenoidal lobe, was explored, with negative result. In two cases nasal sinusitis was treated, in one the antrum and in the other the sphenoid being infected. In 17 cases an autopsy was secured, and in each case confirmed the diagnosis of meningitis. In four of these the internal ear was found infected; in one an unsuspected temporosphenoidal lobe abscess was present; in two there was osteomyelitis of the temporal bone, involving the petrous part in one; in four pus was present in one or more intracranial venous sinuses, and in three there was involvement of the sphenoidal and ethmoidal air cells.

Cerebrospinal fluid findings.— The highest cell-counts recorded were 26,400 leucocytes in a pneumococcal case, and 18,800 in a hæmolytic streptococcal case. Chlorides, where estimated, were always below 700 mgm. per 100 c.c., the lowest being 570 mgm. % the day before death in a streptococcal case. Quantitative sugar estimations were not made, but in all cases in which qualitative tests were performed shortly before death, sugar was greatly diminished or absent.

Quantitative protein estimations were made in most cases, but, as noted by Greenfield, gave no reliable index to prognosis.

One of the three patients who recovered was shown by Mr. Sydney Scott. This was that of a boy suffering from cerebellar abscess, in whose cerebrospinal fluid streptococci were found on more than one occasion. The report on his C.S.F. was: Cells, 484 polymorphonuclears per c.mm.; protein 20 mgm.%; chlorides 560 mgm. %; cultures, streptococci. The other two cases I will describe in greater detail.

I. A boy, aged 7, admitted to hospital on account of vomiting and pyrexia.

Previous history.—Three weeks before admission he had sore throat, followed by earache and headache, with some vomiting.

Five days before admission he attended hospital and was kept in under observation for three days. At that time the left tympanic membrane was red, not bulging, there was some tenderness over the left mastoid process and in the left frontal region, with puffiness of that region and of left upper eyelid. No pus was obtained by myringotomy, and skiagrams showed undeveloped frontal and clear ethmoidal sinuses, and ? opaque left mastoid.

On readmission he was not in pain, and had no otorrhœa, but there was tenderness over the left mastoid. All reflexes were normal and the œdema previously present had disappeared.

Three days after admission the temperature rose suddenly to 103° F. P. 146. Schwartze's operation was performed by Mr. T. H. Just, and disclosed a moderately acellular mastoid, with thickened mucosa and sticky secretion in antrum and cells.

The day following this operation headache and vomiting persisted, and slight head retraction was noted. 5 c.c. C.S.F. were withdrawn, at pressure of 90 mm. water. Report: Cells 800 per c.mm., 66% polymorphs; protein 30 mgm.%; sugar normal; chlorides 670 mgm.%; cultures: 2 colonies staphylococci: probably contamination.

Second day after operation: Vomiting persisted. 30 c.c. C.S.F. withdrawn, 10 c.c. in morning, 20 in afternoon. Report: Cells, very large numbers of polymorphs; protein 160 mgm.%; sugar absent; chlorides 680 mgm.%. Cultures: pure growth of hæmolytic streptococci. Lumbar puncture was performed twice daily for two days, and once daily for a further eight days, averaging 37·5 c.c. per day. Further cultures were sterile.

On the twentieth day after operation he had a convulsion, with conjugate deviation of the eyes, and slow rotation of the whole body. He vomited, and temperature and pulse rose moderately. Cerebellum was explored: but no abscess found; then temporosphenoidal lobe with same result.

Four days later vomiting continued, so 70 c.c. C.S.F. were withdrawn. Report: Cells 78 per c.mm., 62% lymphocytes; protein 60 mgm.%; sugar normal; chlorides 720 mgm.%; cultures sterile.

After this the boy gradually made an uninterrupted recovery.

II. A girl, aged 7½ years. On the sixth day following Schwartze's operation, her temperature rose suddenly. Vomiting and head retraction were present, and Kernig's sign was positive.

Lumbar puncture the following day disclosed turbid fluid under pressure of 250 mm., containing 2,000 cells per c.mm., mainly polymorphs, but with no organisms demonstrable by film or culture.

Treatment was confined to repeated lumbar puncture, and the patient left hospital on the fifty-seventh day after operation. About one year later she came under observation on account of epileptiform attacks, which have since been pronounced functional.

Cases of aseptic meningitis, sometimes known as serous or sympathetic meningitis, have not been included in these statistics. The cerebrospinal fluid in such cases is under increased tension and may be clear or turbid, with increase of protein. Cells are increased from 5 to 500, and may be mainly polymorphonuclears. But the fluid is sterile, the sugar is normal—unless very large numbers of cells are present—and chlorides are normal, or only slightly reduced.

Carmichael examined the cerebrospinal fluid in several cases of lateral sinus thrombosis, one of extradural abscess, and several of cerebral abscess, and found in all cases the above characteristics of an aseptic meningeal reaction.

I wish to express my thanks to Mr. Sydney Scott for permission to use the records of cases under his care at St. Bartholomew's Hospital.

Dr. C. P. Symonds: It has been borne in upon me as I have listened to Mr. Layton and Mr. Jory, that meningitis is not an easy condition to define. Mr. Layton has laid special emphasis upon neck-stiffness as the earliest evidence of meningitis. We should admit the value of this sign when present, but I would submit that its presence depends upon involvement of that part of the meninges which covers the dorsal aspect of the medulla. I have seen two patients with tuberculous meningitis die without any cervical rigidity. In one of these an autopsy was obtained and showed the exudate confined to the cisterna pontis, the cisterna magna having escaped. Again, in cases of meningitis arising from a source of infection in the middle or anterior fossa, one may have symptoms such as headache and vomiting with a turbid spinal fluid before neck-stiffness appears. The absence of this sign, therefore, cannot exclude the diagnosis of meningitis. There are cases in which examination of the spinal fluid provides the first evidence.

The distinction between septic and aseptic meningitis based upon examination of the spinal fluid is, I think, of doubtful value, and may be dangerous. A clear fluid, with moderate increase of cells and protein, may be found when there is a septic focus present from which bacterial toxins only are leaking into the subarachnoid space, or if organisms are gaining entry, they are rapidly destroyed. On the other hand, a similar fluid may contain living bacteria which can be grown on culture. If the distinction between aseptic and septic meningitis is that between an organism-free fluid and an organism-containing fluid, then we should remember that the latter represents an early stage of the former, and that the difference in time may be a matter of a few hours. As Mr. Layton has pointed out, there is not time in these cases to wait for the results of culture.

Mr. Layton has given us a very clear account of the uncomplicated meningitis developing from acute otitis media. This, however, is a type of case which seldom comes within the view of the neurologist except when the middle-ear disease has been missed by the general practitioner. I propose, therefore, in my remarks to cover a wider field, which includes meningitis arising from chronic, as well as from, acute middle-ear infection.

I take it there are three main pathways or modes of progression of infection from middle ear to meninges :—

(1) Directly along thrombosed and infected vessels in the bone which ultimately communicate with those in the subarachnoid space.

(2) More or less directly through the labyrinth, whose fluid communicates with the cerebrospinal fluid.

(3) Step by step through bone, dura, and arachnoid with a reactive process on the part of the newly infected tissue at each step.

In the first two instances the invasion of the subarachnoid space is sudden and may be extremely rapid. When the infection invades through the labyrinth there will be appropriate premonitory symptoms. If the spread is by way of infected vessels there may be none. The symptoms and signs of a diffuse meningitis, as Mr. Layton has described them, may simply be added rapidly to those of otitis media. I suppose, from what Mr. Layton has told us, that this is a common mode of invasion in acute otitis media, and that this is why he has observed neck-stiffness to be the first evidence of meningitis in this group.

As I have said, my experience of these cases is small, but from the study of diffuse meningitis of other origin I should have expected that symptoms such as headache, vomiting, and restlessness might have found a place among the earliest warning signs. When the process of invasion has taken the form of an osteomyelitis with progressive spread through the meninges, I believe that such warning signs are the rule rather than the exception, and would lay especial emphasis on the importance of headache and vomiting, especially if these symptoms are associated with a rise of temperature. It is in such cases, I think, that lumbar puncture may be of value in converting a suspicion into the certainty of early meningitis before neck-stiffness has appeared, providing an indication for exploration and clearance of the infected cavity.

It may be argued that such symptoms as I have described not infrequently occur in the course of convalescence from otitis media, or after a mastoid operation, without the development of frank meningitis. This I expect is true, but in many cases which I have been called to see at a later stage, with extradural or cerebral abscess, I have found an episode of this kind in the earlier history which has suggested that it was at this point of time that the infection first reached the meninges. My suggestion is that the aural surgeon should have the cerebrospinal fluid examined more often in such instances. I do not believe that it is a dangerous procedure.

There are two possible objections to lumbar puncture in such cases. One is that if there be a septicæmia, lumbar puncture may determine the passage of organisms from the blood-stream into the meninges. This fear is based upon experimental and clinical observations published by Wegeforth [1] and others, but considerable doubt has since been cast upon their validity (*vide* Kolmer) [2]. The other objection is that the withdrawal of spinal fluid may lead to the rupture of adhesions and so to the diffusion of a meningitis which has been safely localized. This risk is, I believe, a small one. I have seen one case of extradural abscess in which the sequence of events justified the suspicion that it had occurred.

My desiderata would be that the patient should be within easy reach of the aural surgeon before the lumbar puncture is performed; that not more than 2 c.c. of fluid be removed; that a fine needle should be used, allowing of a slow removal, and that the report should be available within six hours. Cell-count and protein estimation are all that are necessary, and it should not be difficult to get this done. I should like to emphasize the need for a differential count of the cells. The normal cells of the spinal fluid are small lymphocytes. In one case under my care the cell-count was reported by Dr. Greenfield as 3·5 per c.mm., but he added that among the 18 cells counted there were three large mononuclears and one polymorphonuclear. As events showed, this represented the reaction to an extradural abscess with early meningitis.

I am going to join issue with Mr. Layton when he lays stress upon the importance of neck-stiffness and Kernig's sign in prognosis. These signs indicate

the extent of the meningitis rather than its severity. It is not the irritation of the meninges that kills the patient, but the action of the organisms, or rather their toxins, upon the vital centres. Therefore it is the toxicity of the organism that matters, on the one hand, and the patient's resistance on the other.

The points that are helpful in prognosis are the presence and nature of organisms in the cerebrospinal fluid, and the patient's general condition. A brisk reaction of the meninges, as evidenced by a turbid fluid, is not necessarily of bad prognostic import. I have no doubt that we could all provide, from individual experience, examples of this generalization. One in particular comes to my mind—a case seen seven years ago :—

A boy, aged 12, developed an acute left otitis with discharge, on January 18. On January 28 he complained of pain in the back of the neck and his temperature rose to 101°. Subsequently his temperature remained high. There was vomiting, drowsiness, and irritability, and on February 4 he complained of numbness in the left side of his face. On February 5 I found him delirious with high fever, well-marked neck stiffness and Kernig's sign and absent abdominal reflexes. The left corneal reflex was absent and there appeared to be blunting to pin-prick over the left side of his face. There was no swelling of the mastoid or any tenderness except at its tip.

Lumbar puncture gave a turbid fluid under great pressure. I advised that an aural surgeon be called in, but the parents were unwilling to have an operation and the doctor took a favourable view of the case. This was justified by his report written on February 12 : "I am writing this in the bedroom of the boy you saw with me last Saturday. He has completely recovered; all cerebral and spinal symptoms have disappeared, headache, stiffness and photophobia. Temperature has been normal for five days with the exception of two rises to 99°."

I have only to add that this boy remained well; I saw him eight months later on account of a stammer; his ear-drum was healed.

Such cases as this support the opinion of Neumann [3], who says :—

"In analysing the cases (of otitic meningitis) which end in recovery, one might be tempted to believe that it is a matter for the most part of cases of benign meningitis whose recovery would appear to depend rather upon the nature of the affection than the method of treatment."

I am, of course, not suggesting for a moment that Mr. Layton's argument in favour of a complete removal of the factory of organisms is open to criticism. I have quoted my case, together with Neumann's, dictum as evidence only of the fact that prognosis cannot be judged entirely in terms of neck-stiffness, Kernig's sign, or turbidity of fluid. Given an organism of low virulence and a patient with good resistance, the battle may be won.

As to the possibility of recovery in those cases in which there are organisms in the spinal fluid : In the series reported by Neumann in the paper from which I have quoted, of 59 cases with otitic meningitis 22 recovered, and among these 22 there were 6 in which organisms were present. In four they were found in smear and culture, and in the other two in smear only. In three instances the organism is described as a streptococcus, in two as a diplococcus, and in the other as *Streptococcus mucosus*.

Such a report is most encouraging to one like myself who had thought that recovery when organisms could be demonstrated in the fluid was quite exceptional.

It is for such cases that I should be inclined to reserve the plan of frequent drainage of the cerebrospinal fluid. Continuous drainage has been practised and advocated both in this country by Hampson and by Kubie in America, combined with forced fluids by the mouth or hypotonic intravenous saline. In principle the plan appears to be sound. I should, however, be somewhat afraid of secondary infection through the track of the needle, and should imagine that the procedure might impose a considerable strain upon the patient's resistance.

As to the value of intrathecal serum in these cases, I am in doubt. It has one grave disadvantage in that the serum itself causes irritation and congestion of the meninges, with exudation of plasma. The subarachnoid spaces may thus become so full of gelatinous fluid that drainage becomes difficult or impossible.

I should prefer, therefore, to have these patients with severe meningitis treated on the lines which Mr. Layton has advocated—immediate surgical drainage of the infected focus, adequate nursing with forced fluids, and drainage by lumbar puncture twice in the twenty-four hours.

References.—[1] WEGEFORTH and LATHAM, *Am. Journ. Med. Soc.*, 1919, clviii, 183. [2] KOLMER, *Association for Research in Nervous and Mental Disease*, 1931, xii, 500. [3] NEUMANN, *Rev. de Laryng.*, 1934, lv, 1.

Mr. E. Watson-Williams said that he was not able to deal with the subject quite on all fours with Mr. Layton's opening, as that was confined to meningitis following primary acute otitis; whereas in his (the speaker's) experience, meningitis was far more frequently a complication of chronic or recurrent otitis. This might explain the differences between the clinical pictures seen by Mr. Layton and himself. In the first place, he had not recognized the "early" stage of meningitis, in which there was neck rigidity without other signs. Neck rigidity was not pathognomonic of meningitis; one saw it in hæmorrhage, in brain abscess, and sometimes even in uncomplicated otitis media where there was no other evidence of meningitis. Also, one sometimes saw cases in which meningitis was manifest, but there was no demonstrable neck rigidity—cases of supratentorial meningitis. Three years ago he had published a series of twelve consecutive cases of septic meningitis observed during six years,[1] to which he could now add a further seven cases. Severe headache, fever, and usually vomiting, marked the onset of meningitis; in four cases there was certainly no rigidity of the neck when this diagnosis was made (and in three of these the patient died). On the other hand, definite head retraction and a positive Kernig's sign might be seen within a few hours of the onset; out of seven cases in which these signs were present, only one patient had died; these were mostly early cases. Similarly, drowsiness might be an early sign, and was not correlated directly with a bad prognosis.

It was very important to emphasize, as Mr. Layton had done, that when one was confronted with a case of septic meningitis, one should not wait for the results of a pathological report, or animal inoculation, but should have the theatre made ready at once: meningitis was an urgent indication for operation, and the time to operate was as soon as ever it could be arranged. This was, in fact, one of the few surgical emergencies where every hour wasted before the operation diminished the patient's chances of recovery.

He did not believe that there was any objection to diagnostic lumbar puncture, and always had it performed; very valuable information might be thus gained, particularly in the early stages.

Naturally, if *living* organisms were found in the cerebrospinal fluid the outlook was worse: but even patients, comatose, incontinent, and having purulent cerebrospinal fluid containing living cocci, might recover, and the only factor which the surgeon could influence was the interval between diagnosis and operation. Of the nineteen cases to which he had referred: in six cases operation was performed within three days of the onset; all the patients recovered, although clinically three were cases of severe septic meningitis. Of the thirteen not operated on until the third day or later, in three the patients recovered and in ten the patients died, including four whose clinical signs were relatively mild. Could one better illustrate the supreme importance of prompt operation?

[1] "Septic meningitis," *Practitioner*, 1931, ii, 659.

What further measures should one adopt besides such operation on the ear as local features indicated? He had never had the courage—or, perhaps, the energy necessary to assemble the elaborate equipment—to carry out the treatment by transthecal drainage with irrigation of the arachnoid with iodoformized serum or other fluids; and he did not believe that any good was done by such measures or by the injection of disinfectants into the theca. Indeed, he doubted whether intrathecal injection of anti-sera was of much benefit; he certainly would not use mercurochrome thus. He had concluded that the best way to employ drugs was by intravenous injection, and a severe case of meningitis should be treated by giving 40 c.c. of colloidol silver intravenously, just before lumbar puncture. Therapeutic lumbar puncture was carried out daily (he had not attempted more frequent puncture), and enough fluid was drawn off to reduce pressure to normal. In two cases of the most severe and desperate type, following labyrinthitis, he had carried out drainage through the internal meatus (one patient survived). If a patient did not recover when treated thus, he doubted whether any more drastic surgical measures would succeed. The keynote of surgical treatment of septic meningitis was early operation on the ear and repeated lumbar puncture.

Reference.—"Operative treatment of meningitis," *Bristol Medico-chir. Journ.*, 1926, xliii, 160.

The President said that there were two groups of cases with which this discussion was concerned. In the first there was what might be called infection owing to approximation, i.e. a streptococcal infection passing through all protecting tissues and infecting the meninges. The second group included chronic infection by the more generally recognized paths of which Dr. Symonds had spoken. In these matters post-mortem results had been very indefinite, and it was necessary to rely on the findings in cases of cerebrospinal fever. In 1906 Georki published a series of cases, in which he showed that in eleven cases infection took place along the auditory nerve, in one case via the saccus endolymphaticus, and in three cases through the aqueduct of the cochlea.

He agreed with Dr. Symonds that the condition of effusion which some called meningismus was present in a greater number of cases than was generally recognized. He had been told that it took forty-eight hours for cells to come from the meninges into the lumbar region. Some years ago he had seen several cases of cerebrospinal fever, in which the onset of the illness was very acute, and although during the first twenty-four hours the fluid was under pressure, infected cells were not recognized until forty-eight hours afterwards. Did Dr. Symonds consider that increased pressure was a very important sign, or did he favour the practice of not waiting for the appearance of cells? He would also like to know whether Mr. Layton had used serum intravenously in his early cases of meningitis.

Mr. Sydney Scott: As regards Mr. Layton's reluctance to perform lumbar puncture for diagnostic purposes, I am glad to hear that he is less opposed to this invaluable method of diagnosis than I understood him to be.

With reference to neck rigidity: Resistance on the part of the post-cervical muscles permitting the head to be fixed forwards is a most valuable sign, often the first to raise suspicion of lepto-meningitis. It is very rarely absent, though only a few days ago I saw with Mr. Just a patient with proved lepto-meningitis (*Streptococcus hæmolyticus*) who lay in bed with his head on three pillows and flexed forwards.

I agree with Mr. Layton as to the necessity of free drainage of the primary focus, but I have never seen recovery from elaborate methods devised to irrigate the cerebrospinal system, though we have had recoveries (outside Mr. Jory's series) from repeated lumbar puncture.

As regards the operation of translabyrinthine drainage: I have always held this to have a scope restricted to cases of lepto-meningitis following proved labyrinthitis in the earliest stage. I cordially agree with Dr. Symonds' observations that after drainage of the primary infection recovery depends on the virulence of the organisms versus the antibodies produced by the patient.

I think that fatal termination can be ascribed to three processes: (1) increased intradural pressure; (2) accompanying encephalitis; (3) septicæmia. Repeated lumbar puncture aims at defeating the first condition, the others appear to be beyond the scope of surgery unaided by what may be called general medical treatment.

Mr. Jory has asked me to give some details of one of the cases of recovery in his series.

The patient, a boy aged 6, was shown at the meeting of the Section held in March 1934 when other cases of brain abscess were also shown.[1] He was not shown as an example of lepto-meningitis though he had this complication too. The evidence of lepto-meningitis was the presence of streptococci in the lumbar cerebrospinal fluid withdrawn many times during a period of over three weeks, namely: 1st, 14th, 25th July, 1927. On each of these dates the pathologist reported the presence of cocci in the cerebrospinal fluid. Fortunately the boy is perfectly well and quite free from after-symptoms, in spite of the double complication—cerebellar abscess with meningitis.

The statistics quoted are not comparable with some international statistics showing a recovery of something like 60%, perhaps because at St. Bartholomew's Hospital we only record as cases of lepto-meningitis those in which the infection is proved pathologically as well as clinically, not clinically alone.

Mr. Holt Diggle said that it was interesting to note how the pendulum had swung in the matter of treatment of meningitis. Eight years ago, under the stimulation of the work of Eagleton and of Jenkins, several major operations were performed for this very severe complication—e.g. translabyrinthine drainage, thecal drainage with lavage, and even more extensive operations in the way of approach to the foramen magnum. At the meeting at which Mr. Jenkins had discussed the subject, he (the speaker) had still felt that repeated lumbar puncture would be the method of choice, having had two or three recent successes from it.

On the question of therapeutic lumbar puncture, he was to some extent in agreement with Mr. Layton. The otologist's chief function was to cure, not to provide statistics. If a patient had a headache, perhaps with a little vomiting, but with no other clinical evidence of meningitis, one should approach the primary focus in the mastoid and eliminate the sepsis. But why disturb the lumbar theca by reducing the pressure, if there was the slightest chance of thereby spreading the infection? If after forty-eight hours the headache was still present, a lumbar puncture could be done, which would make it possible to decide whether meningitis was present, and whether repeated lumbar puncture should be carried out.

He was interested to hear Mr. Watson-Williams speak of intravenous injection of colloidal-silver salts combined with repeated lumbar punctures. He believed this was a method, adopted by those treating neurosyphilis, in which intravenous injections of arsenical compounds were given, followed by lumbar puncture. He had no knowledge as to results of this treatment, but felt that there was a field for research in order to ascertain whether there was any type of

[1] *Proceedings*, 1934, xxvii, 1674 (Sect. Otol., 143)

antiseptic which could be passed into the cerebrospinal fluid from the venous circulation. The choroid plexus was, of course, very selective in this matter, and possibly few drugs of any value could be thus diffused into the cerebrospinal circulation. In the few cases which he had had, he had relied on the intravenous injection of antiserum, combined with repeated lumbar punctures, in the belief that some of the antiserum would pass over.

Sir James Dundas-Grant said that he was interested in a paper by Dr. Maloens of Brussels,[1] who showed the effects of the intravenous injection of an antiseptic drug preceded by lumbar puncture, whereas drugs injected into the theca found their way quickly to the kidneys.

Mr. C. P. Wilson said he wished to ask Mr. Layton a question, in view of what he said about tying the auricle forwards in order to ensure free drainage of the infected area. To what extent was he prepared to go to ensure free drainage in a case in which meningeal infection was diagnosed? Even in a Stage 1 case did he, in all those cases, carry out a complete mastoid operation? If not, why not? Did Mr. Layton, as a routine, expose the dura mater of both fossæ? If so, how much bone did he remove in order to ensure that exposure? If he did not proceed to that extent, he (the speaker) would like to know why.

Mr. Layton (in reply) said that the request made to him was that he would open a discussion on otitic meningitis, and for that reason he had not included notice of the various cases brought to hospital in which the meningitis had arisen from other parts of the body. As to nose infections, he was in agreement with Dr. Symonds, but he did not think that remarks applicable to the nose could be applied to the ear, or vice versa.

There were twenty different subjects which he had excluded in order that he could concentrate on a clear-cut description of one type of case. One of these was the differential diagnosis of otitic meningitis from meningitis of other kinds occurring in people who had otitis media. There he was in agreement with other speakers as to the value of lumbar puncture. He had not discussed diagnostic lumbar puncture to-day, because in a typical case of otitic meningitis arising from the previously uninfected ear it was not necessary. Though Mr. Sydney Scott appeared to differ from him, both opened the mastoid, and that was the point upon which he (the speaker) insisted. He was not dead set against lumbar puncture, he was against house surgeons and others jabbing needles into the back of little children without due thought as to what they were going to gain thereby. He maintained that the surgeon did not make the patient well. All he did was to put the patient in such a condition that recovery resulted from the unremitting care of the doctor and the nurse, perhaps particularly of the latter. He again emphasized the importance of getting rid of the factory from which organisms were getting in from outside the dura mater to the meninges. He liked Dr. Symond's description of the three kinds of path by which the micro-organisms entered. With regard to the channel from the vessels into the bone, he doubted whether it often occurred without preliminary thrombosis of the lateral sinus. These he would call *the three*

1 "Sur la chimiothérapie postopératoire des méningites purulentes généralisées septique d'origine otitique." *Brux. Méd.*, 1924, **5** (i), p. 81.

lesions of access. In the acute cases the same kind of thing occurred, but these were not complicated by chronic progressive changes, such as fibrosis, and sclerosis of bone.

As to the question of virulence, it was true that, in the end, the virulence of the organism present was the factor which determined whether or not the patient would get well, but in the case which Dr. Symonds had described there occurred that concatenation of unassessable factors called "luck," and the patient had recovered.

With regard to neck-stiffness, he laid more stress on that symptom than most of the speakers appeared to do—probably because he did not feel sure that all observed it when it was present. It was not the same thing as head-retraction. Neck-stiffness could be recognized long before head retraction occurred. It was true that in nasal meningitis one did not encounter it. The two were not comparable symptomatically. He had never seen a case of otitic meningitis in which neck-stiffness was absent. If no neck-stiffness was present in a case of meningitis he would like to know the result of the lumbar puncture. He did not mind the term "meningeal irritation." He agreed that a case, here and there, would get well if left alone. One of his own first cases was that of a small child who was brought into Guy's with a request from the physician that he (the speaker) would perform the mastoid operation, as there was neck-rigidity. He (Mr. Layton) had said that it would be well to do a paracentesis; that was done and the patient got well. He would not follow that course to-day, however, because most of the cases passed from neck-stiffness to Kernig's sign, and then showed the "symptoms and signs of meningitis" as described in the books. If those signs were waited for, the patient would die in the meantime. If a chance for recovery was to be given, operation should be performed when there was neck-stiffness.

With regard to the warning signs given by Dr. Symonds, it was necessary to distinguish between the symptomatology of the lesion of access and the symptomatology of the meningitis. If there was an inflammation of the bone spreading throughout the petrous bone Gradenigo's syndrome might be present with paralysis of the eye. The latter was not a sign of meningitis but if such a patient had meningitis the paralysis of the eye was a sign of the lesion of access which preceded it. If one met with a patient who had labyrinthine symptoms, these latter were not symptoms of meningitis, but of the lesion of access which preceded the meningitis. He thought that was the meaning of the vomiting in the early stage of acute cases. He looked very gravely on vomiting in all children suffering from otitis media. What first made him do so was a series of cases of which Dr. Symonds had taken charge, cases which he (the speaker) had had at fever hospitals and in which late neurological symptoms or complications had developed. In each of those cases there was a note of the child having vomited. It was said that any child was likely to vomit when it was ill. It might do so as a result of acidosis. In a child who had no acidosis, vomiting must be regarded seriously if there was a running ear. It pointed to the need for considering the necessity of exploring the mastoid.

Dr. Symonds (in reply) said that meningococcal cases were difficult ones to argue from, because the first stage of meningococcal meningitis might be entirely septicæmic, so that there would be a normal fluid at that stage, which might be under some increased pressure owing to cerebral congestion. He would be disinclined to accept a pressure-reading as evidence of meningitis unless there was some abnormality in the cells of the fluid.

CASES

Operative Isolation of the Petrous Bone.—E. A. PETERS, F.R.C.S. (President).

Otitic Suppuration. Meningitis. Operation: Isolation of Petrous Bone. Pressure on Nerves vii and viii. Recovery of Nerve viii, and part of Nerve vii.

Leonard B., aged 38.

Previous history.—Three years' history of purulent discharge from the right ear. No pain. Deafness. For one month, attacks of giddiness when standing up or lying down; throbbing in right temporo-sphenoidal region. Occasional vomiting. Bowels opened with medicine.

Condition on admission (30.11.32).—Right ear: granulations, touched with silver nitrate (solid).

Hearing: Right $\frac{25}{30}$ c mast. $\frac{30}{30}$. Left.
Nil. c value of middle ear $\frac{15}{40}$.

Pupils equal; react to light. Horizontal nystagmus on looking to left. Right knee reflex ++, plantar gives flexor response. Abdominal reflexes present. Blood-pressure 155/90. Wassermann reaction negative.

8.12.32: Better. Aural polypi again cauterized.

16.12.32: Temperature 100·4. Pulse 84. Respiration 20. Has severe pain in head. Lumbar puncture: Cerebrospinal fluid under pressure; cells 103 per c.mm.

19.1.33: Lumbar puncture: 1,632 cells per c.mm.; large and small lymphocytes, some polymorphonuclears. No organism on culture.

20.1.33: Lumbar puncture: Cerebrospinal fluid under pressure; total cells, 1,272 per c.mm.

Diagnosis: Meningitis by labyrinthine infection.

23.1.33: *Operation: Isolation of the petrous bone.*—A radical mastoidectomy exhibited some osteitis but no obvious fistula in either the foramen ovale or external canal. The tegmen tympani was removed and the middle fossa exposed; later a packing of b.i.p. ribbon gauze was inserted between the dura and the bone.

The lateral sinus was exposed down to the bulb, and the bone cleared away anteriorly till the dense bone of the canal system was reached. Then, in the area between the inferior and superior petrosal sinus, the dura mater was separated from the bone with a special sharp spoon. The point of the spoon was directed to the internal auditory meatus as located by a view of the outer wall of the internal ear.

The facial nerve became paralysed as shown by loss of tone of the eyelid and it was thought that nerve viii had gone as well. B.i.p. packing was introduced into this triangular extradural space. The middle-ear pus gave growths of coliform bacilli and streptococci.

25.1.33: Cerebrospinal fluid under pressure. Cell count 817 per c.mm.

10.2.33: All the packing removed. Cerebrospinal fluid 44 cells per c.mm.

Patient appeared to be stone deaf with TF c applied to right ear. The hearing has gradually improved in the right ear and at the present time though the c value of the middle ear is nil, bone conduction is equal on both sides. The facial nerve has partly recovered.

There is some giddiness but I have not carried out any labyrinthine tests.

In this operation on a case in which meningeal infection via the labyrinth appeared certain, an attempt was made to pack off the infecting petrous bone, divide nerves vii and viii, separate the saccus endolymphaticus and possibly deal with the aqueduct of the cochlea and petrosal veins by pressure.

Though at the operation nerves vii and viii appeared to be divided, recovery has taken place.

The sheath of the nerve was opened as indicated by a rush of cerebrospinal fluid but complete division could not have been effected; the temporary paresis must have been due to pressure by the plug.

Acute Otitis Media—Acute Mastoiditis—Schwartze's Operation—Onset of Meningitis during Convalescence—Pneumococci from Cerebrospinal Fluid—Recovery.—F. C. W. CAPPS, F.R.C.S.

J. M. was admitted to hospital on March 17, 1930, suffering from acute mastoiditis (right). A Schwartze operation was performed.

18.3.30: Patient developed pneumonia at left base. He progressed satisfactorily until 3.4.30 when he developed pneumococcal meningitis. Sudden onset with neck rigidity while up on couch for the first time. He was treated with immediate and repeated lumbar punctures and replacement of the cerebrospinal fluid by Type 1 pneumococcal antiserum. This was done on speculation as there had been no time to group the pneumococcus.

1.5.30: He was stated to be fit for discharge, but was detained, as the ward was closed on account of diphtheria.

12.5.30: He was sent to the Fever Hospital with Klebs-Löffler bacilli present in his throat. Uneventful recovery.

Mr. CAPPS (in reply to a query) said that in the first three days lumbar puncture was done twice a day, and afterwards it was carried out once a day for the next week.

Bezold's Mastoiditis: Cholesteatoma with Intact Tympanic Membrane.—N. A. JORY, F.R.C.S.

Patient, a man, aged 24, was admitted to hospital on account of a Bezold's abscess.

History.—Swelling and pain in right side of neck for three days. Discomfort and deafness in right ear for four days. Past history of scarlet fever and transient otorrhœa as a child.

On admission.—Right tympanic membrane red, malleus appeared to be fixed, with some swelling of the membrane anteriorly and posteriorly. No perforation; no discharge.

Operation.—A large cholesteatoma was found occupying the mastoid process; this had eroded the posterior wall, exposing the lateral sinus for ¾ in., and had perforated the tip of the mastoid, leading to a Bezold's abscess containing about ʒj pus. The mastoid antrum and aditus were free from cholesteatoma, and the mucosa was only moderately inflamed. No myringotomy performed.

Hearing returned three days after operation, and the tympanic membrane appeared to be normal.

? Acoustic Tumour, ? Ménière's Syndrome: Case for Diagnosis.—MAURICE SORSBY, M.D., F.R.C.S.

Sidney J., aged 54, complains of giddiness and vomiting.

Previous history.—Two years ago he fell off a bus, hitting his head; he was unconscious for a few minutes, but felt quite well afterwards.

Eighteen months ago an "acute peptic ulcer" developed; on several occasions the patient vomited large quantities of blood; he had melæna and felt faint. Five

months ago he became suddenly deaf in the left ear. No obvious cause was found. Four months ago he suddenly became giddy and several times vomited the entire contents of the stomach. The attack lasted two hours and he felt quite well afterwards. He states that he tended to fall to the left side. Three months ago there was an identical attack of sudden onset, and he felt well afterwards.

Since then he has had frequent attacks. Eustachian catheterization during the last three weeks has greatly reduced the severity of these attacks. Lately he has been having dull headaches, and a general heaviness of the head. The sense of taste has become poor.

Condition on examination.—Left facial paralysis; practically total loss of sense of taste for sweet, salt, and bitter; taste for sour is fairly good. Left ear: There is a considerable loss of air conduction, and bone conduction is shortened. Rinne negative and Weber referred to the left side. There is loss of low tones. To the caloric test the affected ear is slightly more sensitive than the healthy ear. Right ear: Air conduction normal; bone conduction shortened. Rinne positive.

There is no other evidence of a neurological lesion.

Discussion.—Mr. SYDNEY SCOTT said he had not seen a case of auditory-nerve tumour in which the caloric reaction was present.

Mr. CAPPS asked whether the Wassermann test had been made in this case.

Mr. SORSBY (in reply) said that the Wassermann reaction was negative and the caloric test elicited a normal response.

Acute Mastoiditis: Meningitis.—T. H. JUST, F.R.C.S.

The patient, a boy, aged 7, was admitted to hospital on account of vomiting.

History.—Three weeks previously had sore throat, followed by earache, left side, and frontal headache. Five days previously was seen to have red—not bulging—drum. Drum incised, but no pus obtained.

On admission.—Tender mastoid. No otorrhœa. No abnormal neurological signs.

Three days later.—Mastoid operation performed. *Day after operation.*—Signs of meningitis. *Second day after.*—Streptococci grown from lumbar puncture fluid.

Repeated lumbar puncture. Recovery.

Temporo-sphenoidal Abscess. Drainage. Recovery.—MAURICE SORSBY, M.D., F.R.C.S.

Rose S., aged 44, admitted to St. Andrew's Hospital, April 4, 1934, complaining of otorrhœa, giddiness, and vomiting.

History.—The left ear had been suppurating for fifteen years; a sense of fullness had been present for the last fourteen days. Vomiting and giddiness had set in three days previously.

Condition on examination.—Profuse, pulsating fœtid discharge from the left ear. Total destruction of the drum, associated with severe deafness; left facial paralysis. Lateral nystagmus to the right. Past-pointing with the right finger.

First operation.—Radical mastoid; a large cholesteatomatous mass removed. The external semicircular canal was found to be eroded. The dura mater and lateral sinus were exposed and found to be normal. Lumbar puncture: Cerebro-spinal fluid was clear and not under pressure.

Pathologist's report (Miss K. M. Collis).—Cells, 7 per c.mm. (lymphocytes); protein, 0·025%; globulin, no excess. No organisms seen in direct film. Culture sterile.

Post-operative history.—After initial improvement, during which the vomiting and giddiness practically disappeared, the patient became worse on April 27 (eighteen days after the mastoid operation). Severe headache developed on the affected side; the temperature rose to 101·6°, the pulse to 110, and drowsiness, rapidly passing into unconsciousness, set in.

Condition on examination.—Dilatation of homolateral pupil; homonymous hemianopia; past-pointing; bilateral papillœdema; optic aphasia; nystagmus to the right; left abdominal reflex absent; left knee-jerk accentuated; plantar reflexes flexor.

Second operation: Temporo-sphenoidal lobe explorations.—The original operation wound was reopened: the dura was found bulging. On exploration with a needle, pus was found at a depth of three-quarters of an inch. (Culture: *Staphylococcus albus*, pneumococci, and *B. proteus.*) The dura was incised, and the abscess was drained and a drainage-tube inserted. Lumbar puncture: fluid clear; under pressure.

Post-operative history.—Consciousness soon returned, and the patient was able to recognize people and objects; the papillœdema slowly subsided. On May 4, however (eight days after the second operation), the drainage from the abscess practically ceased and the patient again became drowsy. She could be aroused with difficulty and took no food. The temperature remained normal, but the pulse was slow, varying between 60-70. Lumbar puncture: Cerebrospinal fluid slightly yellow; a little blood present; protein 0·08%; globulin present in excess; chlorides, 770 mgm. per 100 c.mm. Cells, 70 (practically all lymphocytes) and 150 red blood-cells per c.mm. No tubercle bacilli found; culture sterile.

The drainage-tube in the abscess cavity was manipulated, and a great flood of pus was obtained. The drowsiness soon disappeared and the patient made an uneventful recovery.

Streptococcal Meningitis secondary to Acute Suppurative Otitis Media: Simple Mastoidectomy. Recovery.—E. WATSON-WILLIAMS, M.C., F.R.C.S.Ed.

Eva B., aged 49, complained on July 2, 1933, of pain in and behind the right ear, and in the throat, during three days, after a bad cold; had never had any previous ear disease. The day before admission she was giddy, walking towards the right, and seeing "things go round clockwise." On the day of admission she was very giddy, and vomited several times. The ear had begun to discharge thin bloody serum, and was painless, but she had a terrible neuralgic headache (subject to this) across the front of the head. Quite sensible, but drowsy, and preferred to lie on the right side; slight right facial weakness; well-marked rigidity of neck, no ataxia, no past-pointing; plantar reflexes normal, right knee-jerk normal, left absent, pupils normal. Tuning-fork not heard at all at meatus; on mastoid heard less well than normally. Weber referred to left. Rather slow, coarse mixed nystagmus to left. Temperature 102° F.; pulse 100. Caloric test, water at 107° F. in right ear; after 2′ 40″ horizontal nystagmus to right on looking to right, but still some mixed nystagmus to left on looking to left. Lumbar puncture; pressure much raised, fluid turbid. Report: "Purulent fluid containing pus cells and streptococci." Later, streptococci cultured. Immediate operation, right simple (Schwartze) mastoidectomy. The bone was of very cellular type, dripped blood; cells full of old blood; at tip some contained a little thin sero-pus; antrum empty. Lateral sinus, dura apparently normal. (Streptococci grew from pus.) "Bipp" and loose dressing; 30 c.c. antiscarlatinal serum intramuscularly.

July 3: General condition unchanged; very thirsty; nystagmus, facial paresis less; temperature 100° F. Lumbar puncture, after intravenous injection of 40 c.c. collosol argentum; magnesium sulphate per rectum. July 4: Same treatment. July 5: Enormously better, temperature 99·2°. No headache, little neck rigidity. July 6: Treatment as on July 3. Convalescence uneventful.

September 1934: Healed; some deafness and humming tinnitus on right side.

November 1934: No change; still has severe headaches at times as before the attack: recent exploration of nasal sinuses negative.

Section of Radiology

President—F. HERNAMAN-JOHNSON, M.D.

[*November* 16, 1934]

Some Problems in Diagnosis and their Solution by Radiologic Examination of the Alimentary Canal

By B. R. KIRKLIN, M.D.

(*Section on Roentgenology, The Mayo Clinic, Rochester, Minnesota*)

IT would be advantageous if every patient with more or less chronic symptoms that might possibly have their origin in gastro-intestinal disease could be subjected to radiologic examination of the digestive tract. Under present circumstances, however, it is impracticable to apply this test in every case, on the mere chance that it might yield important information. One obstacle is that it would often add needlessly to the cost of medical care. Another is that competent radiologic service is not always near at hand and the patient would have to be sent to a distant place where it could be obtained. Consequently, the clinician ordinarily feels obliged to request this examination only when he is confident that it will elicit significant data, or when the combination of signs and symptoms is typical, or strongly suggestive, of a gastro-intestinal lesion. But this fails to make provision for atypical cases and for patients who have only a few vague symptoms but are nevertheless in the early stages of grave disease. For several years the medical profession has sought, through the press and by radio broadcasts, to impress the public with the necessity of seeking medical counsel concerning all symptoms, however trivial they may seem, in order that malignant growths may be discovered at a time when there is still a chance for cure. This imposes a special obligation on physicians to find existing cancers at the earliest opportunity and it is only with the X-ray that most of the early cancers of the alimentary canal can be discovered. Similar considerations apply to certain non-malignant diseases which can be treated with greater success early than late.

For these reasons, the basis of selecting patients for radiologic examination should be sufficiently broad to include all those whose symptoms are at all indicative of chronic organic disease of the alimentary tube, unless such disease can rather confidently be excluded, or unless the condition of the patient forbids the examination. This basis cannot be prescribed in exact terms and would be formulated differently by different physicians, in accordance with their particular experiences, but there are certain clinical manifestations which, even when not pronounced or not associated with their common accompaniments, should be regarded as imperative signals for thorough investigation with the X-ray unless the cause is obvious or can readily be determined by other means. Such signals include (1) hæmorrhage from the alimentary canal; (2) anæmia; (3) marked and rapid loss of weight; (4) repeated attacks of nausea or vomiting; (5) persistent abdominal pain, or recurring epigastric pain or distress related to food; (6) constipation associated with abdominal pain, constipation alternating with diarrhœa, or chronic diarrhœa, and (7) vague, atypical abdominal symptoms for which no definite cause can be found. Inasmuch as I am not a clinician, I shall consider these symptoms and signs only in relation to their significance as signals for radiologic examination.

HÆMORRHAGE

Hæmorrhage from the alimentary canal, whether in the form of gross hematemesis, blood-stained vomitus, frank bleeding from the bowel, or tarry stools, is an urgent indication for radiologic investigation. Peptic ulcer is so often the cause of such hæmorrhage that only this lesion may be considered by the clinician, and I have known instances in which the radiologist, prejudiced by the history of hæmorrhage, made a diagnosis of duodenal ulcer when the lesion was quite different both in character and situation. As illustrations I shall cite a few cases in which hæmorrhage was the sole or dominant symptom, and its source was first established by means of the X-ray.

A man, aged 26, came to the Mayo Clinic for radiologic examination, chiefly because he had had gastro-intestinal hæmorrhages. Three years previously he had vomited blood and had noted the presence of blood in the stools. Following a diet of milk and soft foods, the bleeding had ceased. A year later he had had a similar attack, from which he had recovered, and thereafter had gained weight. Physical examination and tests disclosed severe anæmia,

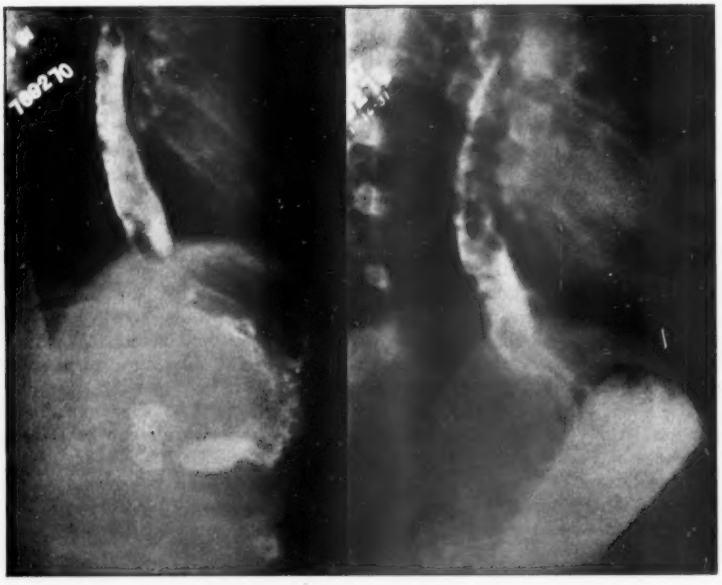


FIG. 1*a*. FIG. 1*b*.

FIG. 1.—Extensive varices of the œsophagus. *a*, Characteristic mottling caused by varices; *b*, mucosal study showing the typical appearance of œsophageal varices.

with leukopenia and definite enlargement of the spleen. The concentration of bilirubin in the serum was increased, and the van den Bergh reaction was direct. The whole clinical picture seemed to fit best with cirrhosis of the liver secondary to splenomegaly. Radiologic examination, after administration of a suspension of barium, disclosed multiple shadow-defects in the lower half of the œsophagus that were typical of varices (fig. 1*a*). This diagnosis was confirmed by œsophagoscopy (fig. 1*b*). Splenectomy was performed. The spleen weighed 800 grm., and the pathologic diagnosis was as follows: Marked chronic splenitis with perisplenitis; splenic anæmia; progressive Banti's disease.

Œsophageal varices are rather rare, but in the few published reports of radiologic observations, remarkably similar appearances have been described and illustrated. When a few swallows of the barium mixture are taken, the shadow of the lower segment of the œsophagus is so distorted that usually the examiner thinks first of cancer. But obstruction is lacking and the characteristic, multiple, rounded, transradiant defects in a reticulum of shadow become evident. Even then the radiologist will be inclined to attribute them to multiple polypoid new growths, for they have a striking resemblance to such growths in the stomach. However, œsophageal polyps seem to be less common than varices, and when the latter are once seen, they are readily recognized thereafter.

Another case in point, but of a different kind, was that of a woman, aged 49, who, in the course of an attack of sick headache one month previously, had vomited several times and had ejected a mouthful of bright red blood. A few similar hæmorrhages occurred subsequently. She was a widow, with three dependent children, and she was greatly worried

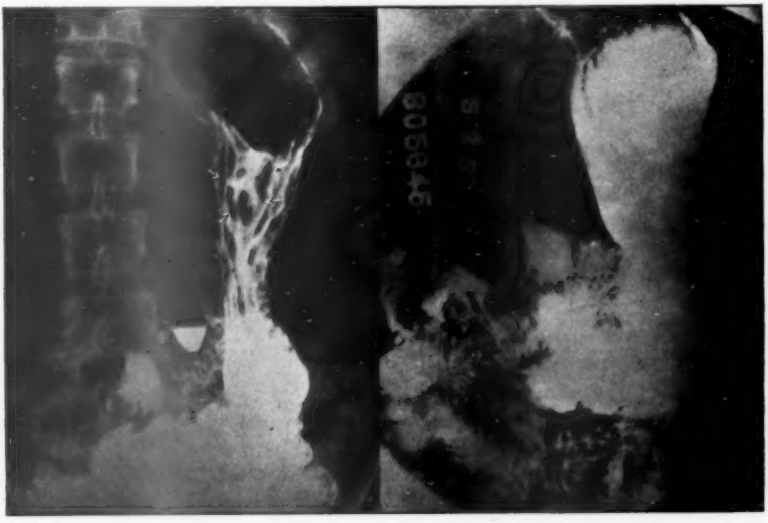


FIG. 2*a*. FIG. 2*b*.

FIG. 2.—Sessile adenomatous polyp. *a*, Mucosal study showing large ulcerated polyp, posterior wall, cardiac end of stomach, indicated by arrows; *b*, stomach completely filled, obliterating evidence of the polyp.

by the fear that she had cancer. A radiologic examination made at the request of her physician had been negative. When she came to the Clinic no additional significant clinical data were obtained. On radiologic examination a small, slightly ulcerated, sessile polyp, considered benign, was found on the posterior wall of the cardiac portion of the stomach (fig. 2 *a*, *b*). At operation the stomach was opened and the polyp was excised. The pathologist reported that it was a sessile, adenomatous polyp, 2 cm. in diameter, and that on its surface was a small area of ulceration.

Here it may be emphasized that unless the radiologic examination is so executed as to permit direct frontal inspection of the mucosal relief, small lesions of the stomach, whether tumefactive or ulcerative, will almost certainly escape observation. This fact was realized early by Holzknecht who began examination when the first

swallows of the opaque medium were taken, and, after the stomach was filled, he compressed and thinned out the contents so that the mucosal topography could be looked at directly. Holzknecht's many followers have not failed to observe this detail. However, as the majority of lesions are sufficiently large to deform the profile of the barium shadow, not all radiologists have fully appreciated the necessity of obtaining a surface view to discover the minority of minute lesions or to assist in the differential diagnosis of larger ones. Hence, in reviving this subject, in pointing out the significance of delicate alterations of the internal relief in the discovery and identification of disease, and by devising refinements of technic whereby such changes can be demonstrated with facility, Berg and Akerlund have rendered great service to radiologic diagnosis.

Again different was the case of a man aged 34, who for ten years had had attacks of bleeding from the rectum, in the form of dark clots. The attacks had usually followed catharsis or hard work. As the bleeding had been attributed to hæmorrhoids, these had been removed five years before, but the discharge of clots had continued. At the Clinic, on radioscopic examination of the colon with an opaque enema, nothing abnormal was found

FIG. 3*a*. FIG. 3*b*.

FIG. 3.—Adenocolloid carcinomatous polyp of the colon. *a*, Radiogram made after evacuation of barium enema and insufflation of air, showing a rounded shadow-defect in lower descending colon produced by a sessile polyp; *b*, the specimen.

but after evacuation of the enema and insufflation of the colon with air, the radiograms disclosed a small polyp in the lower portion of the descending colon (fig. 3*a*). The patient refused operation at that time. He returned a year later and examination of the large bowel was repeated, with the same results. At operation the portion of the colon containing the tumour was resected. The pathologist reported that the growth was a sessile, adenocolloid carcinomatous polyp measuring 4 by 3·5 by 2·5 cm., and that the lymph nodes were involved (fig. 3*b*).

This case illustrates the importance of employing the combined, or double-contrast, method to exhibit small polyps, and at the Clinic it is consistently applied in all cases of hæmorrhage from the bowel, unless the lesion is demonstrable with the opaque enema alone.

Anæmia

Potential causes of anæmia are so numerous that this is one of the most perplexing signs with which the clinician has to deal, and when it is not accompanied by other manifestations, discovery of its origin often entails laborious investigation. Anæmia of moderate degree seems less urgent in its demand for inquiry, and is likely to be ascribed to a deficient diet or to unhygienic conditions, although it may have much graver causes. Marked anæmia will stimulate a vigorous search for its cause, but it is hard to determine the most promising order of approach, or to keep in mind the uncommon lesions that may underlie the condition. Among such lesions are the primarily benign, polypoid new growths in the stomach or bowel. As a rule, they become superficially eroded, and a slight but constant seepage of blood ensues, with resulting anæmia. In every case of unexplained or seemingly idiopathic anæmia, radiologic study of the gastro-intestinal tract should be made.

For example, a man aged 54 had noticed increasing pallor and weakness for two years, together with tingling sensations in his hands and feet, eructations of gas after meals, and attacks of sore mouth. His physician at home had diagnosed pernicious anæmia. At the Clinic, examination of the blood revealed the features typical of pernicious anæmia. The total

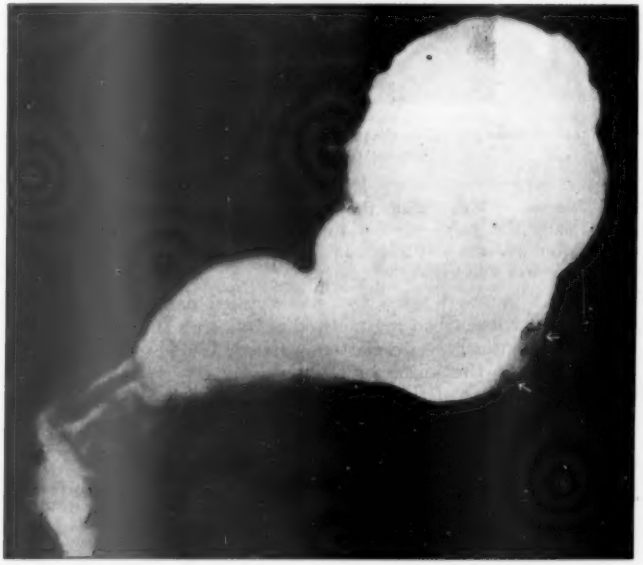


Fig. 4.—Adenocarcinomatous polyps of the stomach. Defects on greater curvature, middle portion of stomach, indicated by arrows, suggesting benign polyps.

gastric acidity was 4, and free acid was absent (Töpfer's method). On examination of the stomach with the X-ray, made as a routine because of the anæmia, two small polyps were found on the greater curvature (fig. 4). At operation the polyps were excised, and the surgeon noted that they bled profusely on the slightest manipulation. One of the polyps was 2·5 cm. in diameter; the other, 1 cm. in diameter (fig. 5). The pathologist reported that they were adenocarcinomas of low malignancy.

A clergyman, aged 65, came to the Clinic for general examination to determine the state of his health, although he had not noted any definite symptoms of disease. On examination

of the blood, slight anæmia was found. Apart from the presence of hæmorrhoids, there were no physical signs of disease. After close questioning, the patient said that for two years he occasionally had seen a little blood in the stools, but had assumed that it came from the hæmorrhoids. Radiologic examination of the colon, which is required at the Clinic as a routine in such cases, demonstrated a small polypoid tumour in the proximal segment

FIG 5.—Specimens of same growth as that represented in fig. 4; pathologic diagnosis was grade 1 adenocarcinomatous polyps.

of the sigmoid flexure. At operation the tumour was removed through an incision in the bowel. Pathologically the polyp proved to be an adenoma, and measured 2 by 1·5 cm. One year later the patient returned in excellent physical condition, and radiologic examination of the bowel was negative.

Exhibition of the mucosal relief was not applied consistently to examination of the colon until Fischer described his method of inflating the bowel with air after the opaque enema had been largely evacuated. Later, Weber introduced certain modifications that enhanced the value of the procedure. By this so-called combined method the internal surface of the intestine retains a thin coating of barium and can be inspected minutely throughout, in stereoscopic radiograms of the air-distended bowel. The method is indispensable for demonstration of small polyps and shallow ulcers; lesions of neither of these types are likely to be visible when the colon is completely filled with the enema.

LOSS OF WEIGHT

Marked loss of weight, without other subjective or objective manifestations of ill-health, is sometimes regarded lightly by the patient, especially if he is of middle-age and has been heavier than he wished to be, or if he expects to grow thin with advancing age. Few physicians will underestimate the potential gravity of this sign, but in the absence of gastric or intestinal symptoms it may seem illogical to give first or serious consideration to cancer of the stomach or colon among the many possible causes. Nevertheless, the onset of such cancers is insidious, and is so often heralded solely by loss of weight, that radiologic examination should be among the first tests applied. Both surgeons and clinicians have repeatedly emphasized that the only way in which most cancers of the alimentary canal can be diagnosed early is by competent radiologic examination.

An instance is furnished by the case of a woman, aged 70, whose weight declined 24 pounds (10·9 kg.) in three months. This was her chief concern, although on inquiry it was learned that for three years she had had slight, indefinite pain in the right hypochondrium and discomfort from gas, especially after the evening meal. The total gastric acidity was 54; free, 32. The radiologist discerned a duodenal ulcer and a small ulcerating tumour, obviously malignant, on the posterior wall, near the lesser curvature, at the angle of the stomach. At operation, extensive involvement of the lymph-nodes was found, but the new growth, together with four-fifths of the stomach, was excised. The lesion was 4 by 3 by 2 cm. in dimensions and, microscopically, was a highly malignant adenocarcinoma.

A loss of 25 pounds (11·3 kg.) was likewise almost the sole complaint of a man, aged 46, although lately, for a few weeks, he had occasionally had sour stomach and epigastric fullness due to gas, and his appetite had become less keen. The total gastric acidity was 10. The value for hæmoglobin was 75 per cent. By radiologic examination an ulcerating cancer at the pyloric end of the stomach was found. It was causing some obstruction, and was considered to be operable. The surgeon reported that the cancer had perforated the posterior wall, against the pancreas, but that no metastasis was evident. Microscopically the lesion was found to be an adenocarcinoma, and was graded 3, on a scale of 4, as to malignancy.

Vomiting and Nausea

Recurring vomiting, without any obvious reason, such as sick headache, is such an emphatic indication for radiologic study that it will seldom be ignored. The X-ray may disclose gastric cancer, ulcer on the lesser curvature with pylorospasm, duodenal ulcer, or an obstructive lesion at the gastric outlet. If the stomach and duodenum prove to be normal, cholecystography may reveal disease of the gall-bladder. On the other hand, nausea, especially when slight, is not an impressive symptom, yet it may be the sole indication of serious disease of the stomach.

A physician, aged 49, came to the Clinic, primarily for diagnosis and treatment of cardiac disease. A year previously he had had severe pain in the thorax, for relief of which administration of morphine had been required over a period of ten days. A diagnosis of angina pectoris had been made at that time. For the past six months the patient had been unable to carry on his work, and during this period he had rather persistent nausea, which had been especially noticeable when his stomach was empty. The cardiologists of the Clinic confirmed the diagnosis of angina pectoris with coronary sclerosis, but because the patient was somewhat anæmic, and more especially because of the persistent nausea, they sent him for radiologic examination of the stomach. This revealed a small ulcerating cancer near the pylorus. On surgical exploration it was found that perforation against the lower surface of the liver had occurred, and, in view of this and of the additional risk entailed by the coronary sclerosis, resection of the gastric lesion was not deemed feasible. After recovery from the exploration the patient returned home, resumed his practice and gained weight, although he continued to have pain, attributed to the coronary insufficiency. Two years later he died. At necropsy extensive cancer of the stomach, with metastasis to the peritoneum, was found.

Epigastric Pain

Epigastric or upper abdominal pain or discomfort that is precipitated, aggravated, or relieved by taking of food, is so strongly suggestive of gastric, duodenal, or cholecystic disease that it will almost invariably receive due attention. This symptom in conjunction with other clinical data will often distinguish between peptic ulcer and disease of the gall-bladder, but clinical distinction between gastric ulcer and duodenal ulcer, or between benign and malignant ulcer, is much less accurate than that obtainable with the X-ray. Further, epigastric distress, related or unrelated to food, is sometimes due to diaphragmatic hernia, which can scarcely be diagnosed without the X-ray. An attack of acute pain may indicate perforation of a peptic ulcer, but when this is believed to have occurred, radiologic examination should be conducted cautiously, without manipulation and, if possible, without administration of barium.

For fifteen years, a woman, now aged 53, had had attacks of epigastric pain and discomfort that had been somewhat suggestive, but not typical, of peptic ulcer. On three widely-separated occasions she had observed blood in the vomitus. In the course of the

fifteen years, she had been subjected to appendectomy, cholecystotomy—at which operation gall-stones were not found as suspected—and, finally cholecystectomy, each for relief of her symptoms. When she was examined at the Clinic with the X-ray, the crater of an ulcer in the second portion of the duodenum, 5 cm. from the pylorus, was discerned. The duodenal bulb was of normal appearance. The diagnosis was confirmed at operation.

Another patient, a man aged 39, had had symptoms and signs typical of peptic ulcer, for fourteen years. Total gastric acidity was 64; free acidity, 52. The radiologic diagnosis was diffuse duodenitis (fig. 6). Gastroduodenostomy was performed, and the diagnosis was confirmed by the pathologist.

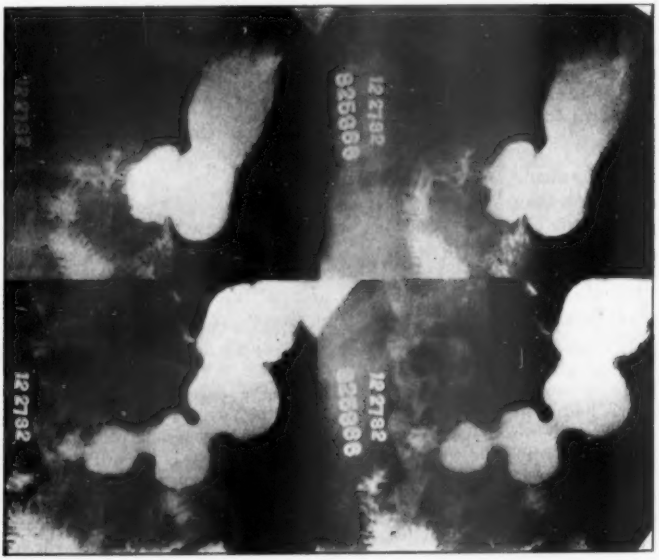


FIG. 6.—Diffuse duodenitis. Mucosal pattern showing coarsely irregular network surrounding translucent areas of the duodenum associated with marked spasm.

Pathologically, duodenitis is characterized by localized or diffuse leukocytic infiltration and œdematous thickening of the duodenal wall, hyperplasia of Brunner's glands, and small, shallow erosions of the mucosa, without definite craters. It may occur independently, or in association with frank crateriform duodenal ulcer. Clinically, the symptoms of duodenitis are somewhat like those of ulcer, although they are often less typical, but the differences are not sufficient for clinical distinction of one from the other. Most striking among the radiologic signs of duodenitis is the extraordinary irritability of the bulb. A suspension of barium races through the bulb so rapidly that there is scant opportunity to inspect the shadow. The bulb is small and grossly deformed on both borders, and the configuration of the deformity changes quickly from moment to moment. The mucosal pattern is coarsely and irregularly reticular, with translucent islets lying in a denser network (fig. 6).

Attacks of distress in the epigastrium in the past four years, with temporary relief from taking of food or soda, were the essential features in the anamnesis of a man aged 48. With the X-ray a penetrating ulcer, 2 cm. or more in width, was found on the lesser curvature. The curvature was contracted, producing the so-called snail form of stomach, antral spasm was marked, and the ulcer was sensitive to pressure. Because of these characteristics and

the convergence of the rugæ toward the crater, the ulcer, although large, was deemed to be benign (*see* Table). This diagnosis was confirmed by operation and microscopic examination.

ROENTGENOLOGIC CRITERIA OF BENIGN AND MALIGNANT GASTRIC ULCERS

Benign	Malignant
Niche usually less than 2 cm. in diameter.	A niche exceeding 2·5 cm. in diameter strongly suggests malignancy.
Niche regularly hemispherical; dense; margins sharply defined.	Niche often conical or irregular; faint; margins poorly defined.
Ulcers on lesser curvature, not near pylorus.	Ulcers on greater curvature almost invariably malignant.
	Ulcers on posterior wall likely to be malignant.
	Ulcers near pylorus open to suspicion.
Gastric peristalsis likely to be active.	Peristalsis often diminished or absent.
Spastic manifestations common:— Narrowing of antrum. Curling of antrum. Hour-glass contraction.	Spastic manifestations rare.
Rugæ commonly accentuated and converge toward niche.	Rugæ adjacent to niche often faintly marked or effaced.
Pylorus spastic.	Pylorus gaping.
Localized tenderness over ulcer.	Ulcer seldom tender to pressure.

Over a period of five years, a man aged 55 had had autumnal attacks of indigestion, with pain in the upper portion of the abdomen, which had begun from two to four hours after meals and had been relieved by taking of food or soda. Recently his weight had declined slightly, but as he had an adenomatous goitre, with hyperthyroidism, the loss of weight was attributed to the goitre. The total gastric acidity was 62; free acidity, 48. The basal metabolic rate was high. With the X-ray, a shallow ulcer on the lesser curvature, above the angle of the stomach, was seen. On examination two weeks later, the ulcer was, apparently, slightly smaller, but the shadow of the crater was indistinct, irregular, and not tender, and there were no signs of gastrospasm. Accordingly the radiologic diagnosis was malignant ulcer. When the ulcer was excised at operation it appeared macroscopically to be benign, but microscopically it proved to be an adenocarcinomatous ulcer of malignancy graded 3.

Although it is known that relative youth is not incompatible with the presence of cancer, the fact is difficult to realize, and reminders are always timely.

Burning epigastric pain during the past four years was the chief complaint of a man aged 31. The pain came on several hours after meals and was relieved by taking of food or soda. Two years before, a radiologic diagnosis of gastric ulcer had been made. Dietetic and other treatment for five months had given little relief. At the Clinic, radiologic examination disclosed a small ulcerating carcinoma on the lesser curvature (fig. 7 *a*, *b*). On surgical

FIG. 7*a*. FIG. 7*b*.

FIG. 7.—Small ulcerating carcinoma of the stomach. *a*, Radiogram showing defect on lesser curvature just below angle of stomach; *b*, drawing of the fluoroscopic images with pressure exerted by palpating hand depicting the typical meniscus-sign complex which is characteristic of small ulcerating carcinoma.

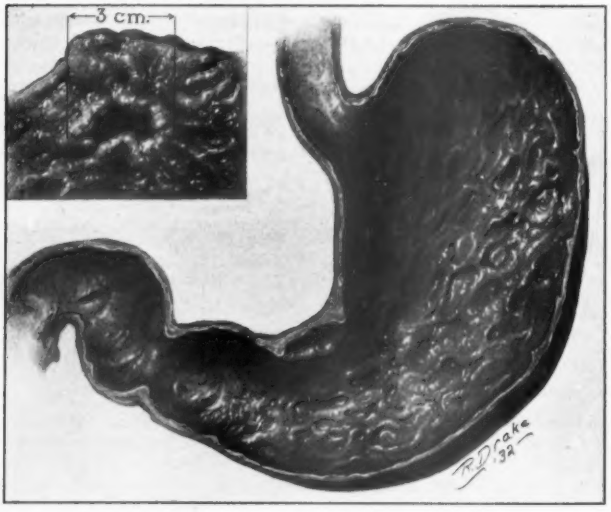


FIG. 8.—Specimen from case represented in fig. 7.

exploration the lesion appeared to be benign and the surgeon proposed to excise it, but the radiologist, who was present, insisted that it was malignant. Yielding to this insistence, the surgeon resected a considerable portion of the stomach along with the lesion. The latter was described by the pathologist as a shallow ulcer, 1 by 3 cm. (fig. 8), which appeared, grossly, to be inflammatory but microscopically was found to be an adenocarcinoma.

On casual observation, a small, ulcerating cancer without obvious tumefaction, resembles a simple ulcer, but on closer inspection the former presents characteristics that enable its distinction from benign ulcer and are practically pathognomonic. Underlying its distinctive signs is the fact that in these malignant lesions tumefaction persists in a degree sufficient to form an elevated border around the ulcerous excavation. If the cancer is on the lesser curvature the ridge appears, under pressure, as a semicircular clear stripe separating the shadow of the barium-filled crater from that of the stomach. If the lesion is on the posterior or anterior wall, the ridge is seen, under manual pressure, as a transradiant halo about the dense shadow of the crater (figs. 7*b* and 12*b*). Further, the crater, being excavated, at least partly, in neoplastic tissue, is not likely to project much, if at all, beyond the normal confines of the gastric lumen; it is not sensitive to pressure and gastrospasm is conspicuously absent.

A woman aged 72 had had attacks of indigestion with epigastric pain and soreness for the past twenty-five years. For a year the distress had occurred after every meal and sometimes had been relieved by vomiting. Occasionally dyspnœa had been associated with the attacks. They had been attributed variously to disease of the gall-bladder, gastric ulcer and gastric cancer. Radiologic examination at the Clinic revealed hernia of about a fifth of the stomach through the diaphragm, at the œsophageal hiatus. Apparently the hernia was incarcerated and there were signs of a lesion in the constricted portion. The diagnosis was confirmed at operation, by which the hernia was reduced, and the dilated hiatus was restored to normal size. The subsequent history indicated that the lesion at the point of constriction was a traumatic ulcer producing an inflammatory mass. Two years later the patient was in excellent health and had gained 15 lb. (6·8 kg.).

For a year a woman aged 58 had had epigastric distress two or three hours after meals. The complete anamnesis and physical findings were suggestive partly of gallstones and partly of peptic ulcer. Gallstones and a small annular lesion at the pylorus, diagnosed by the examiner as cancer, were found with the X-ray (fig. 9). At operation the gallstones were duly present, but the annular constriction at the pylorus was the result of hypertrophy of the pyloric muscle, not of carcinoma.

With interest aroused by this particular mistaken diagnosis, the radiograms in a series of cases of pyloric hypertrophy encountered at the Clinic were reviewed, in order to learn whether or not the hypertrophy might have any marks of distinction from its simulants, namely, prepyloric annular carcinoma, early gastric syphilis, and prepyloric ulcer with spasm. All four affections produce more or less concentric narrowing of the prepyloric segment and are likely to be confounded.

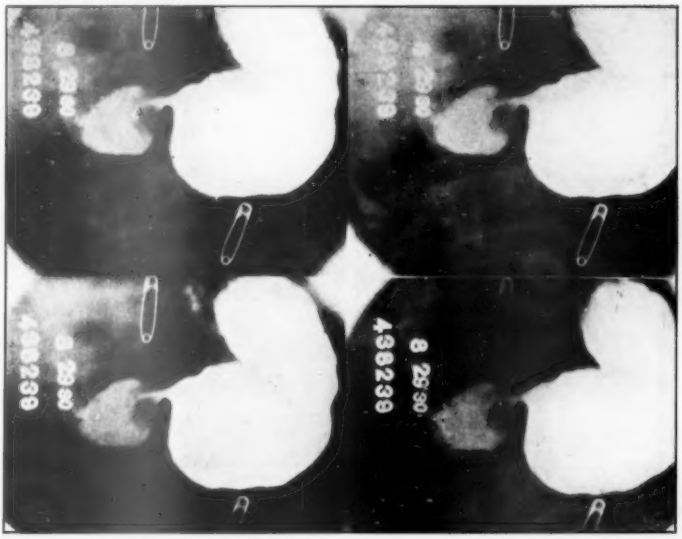


FIG. 9.—Hypertrophy of the pyloric muscle. Typical radiologic appearance of hypertrophy of pyloric muscle showing canalization; crevice on greater curvature side of canal produced by cleft between the pyloric and prepyloric muscle bundles, and crescentic deformity at base of duodenal bulb caused by pressure of thickened muscle.

On reviewing the radiograms it became evident that pyloric hypertrophy has two distinctive features, seldom if ever found in the other diseases. The first is a slight invagination of the bulbar base, which is thus rendered concave, and the shape of the bulb resembles that of a mushroom. Prior to this observation, at least one pathologist had noted that the hypertrophied muscle actually elongates the pyloric canal and is thrust partially into the bulbar base. The second characteristic is a distinct cleft in the inferior border of the elongated canal, about at its middle. As you are doubtless aware, the anatomic basis of this cleft has recently been established by Twining. On the basis of at least one of these two signs, in combination with prepyloric canalization, we have been able to make the diagnosis in several cases, and in some of them it has been confirmed surgically.

An uncomfortable sensation of fullness in the stomach, with an apparent diminution of gastric capacity, was the sole symptom related by a man aged 62. During the previous year, several examinations with the X-ray had been made, and on each occasion the diagnosis had been cancer at the outlet of the stomach. In consequence, the patient had

worried greatly. The total gastric acidity was 42, free acid 30. Loss of weight was slight. By radiologic examination the presence of hypertrophy of the pyloric muscle, typical in every respect, was demonstrated (fig. 10). Operation was discouraged, but the patient, still fearing that he might have cancer, insisted on exploration. At operation the surgeon concurred in the diagnosis. Pyloroplasty was performed. After examining a section of tissue removed for the purpose, the pathologist reported that it was hypertrophied muscle.

Distress in the upper part of the abdomen, caused by bloating with gas, unrelated to meals, was the principal complaint of a woman aged 39. The distress had been noted for

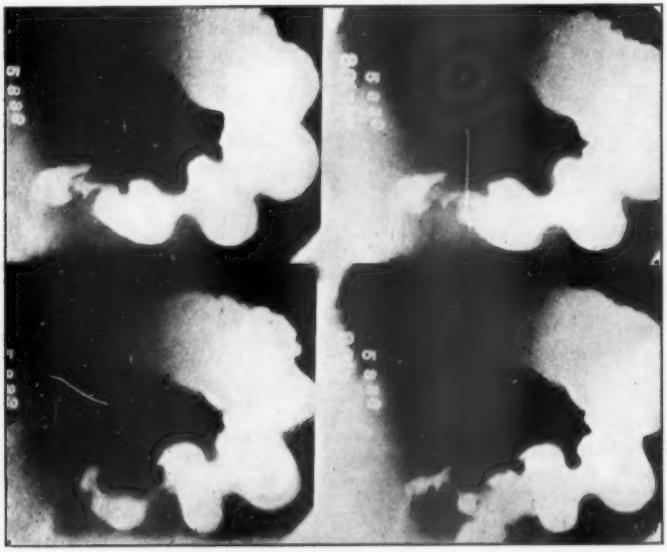


FIG. 10.—Simple hypertrophy of the pyloric muscle showing the three characteristic radiologic signs of the condition.

ten years and had been worse during the past three years. The total gastric acidity was 50, free acids 40, and there was some gastric retention. The concentration of hæmoglobin was 55%. Radiologic examination disclosed two small ulcers on the lesser curvature, above the angle of the stomach, and marked hypertrophy of the pyloric muscle. Two weeks later, after medical treatment, the ulcers had disappeared. The pyloric hypertrophy was, of course, unchanged.

CONSTIPATION AND DIARRHŒA

In cases of ordinary constipation the X-ray rarely elicits any important data. But constipation alternating with diarrhœa may result from obstructing carcinoma or diverticulitis, or such lesions may give rise to intermittent attacks of constipation with pain, and either combination invites radiologic aid. Chronic or recurring diarrhœa calls urgently for radiologic investigation of the colon; chronic ulcerative or tuberculous colitis may thus be revealed.

A history of constipation for several months, together with marked abdominal pain, certainly demands thorough investigation.

A man aged 44 had been severely constipated for more than a year. During the last four months the constipation had been accompanied by attacks of abdominal cramps, and red blood was noted in the stool at these times. The count of red blood cells and the

hæmoglobin was normal. Examination with the combined method disclosed a polypoid tumour in the distal loop of the splenic flexure (fig. 11 *a*, *b*). It was attached by a broad base to the posterolateral wall. The tumour-bearing portion of the flexure was resected. Histologically, the tumour, which was 5 by 5 by 1·5 cm. in dimensions, was an adenocarcinoma, graded 2 as to malignancy. No involvement of the lymph nodes was found.

Even a short history of abdominal pain may be significant. A woman aged 44 had been well until one week before her registration at the Clinic. At that time she had had an attack of severe pain low in the abdomen, followed by bleeding from the rectum, and thereafter movements of the bowel had been accompanied by slight hæmorrhage. At proctoscopic

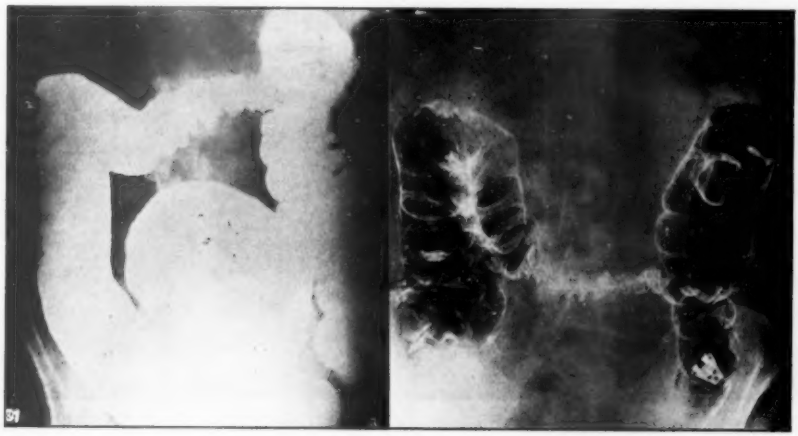


FIG. 11*a*. FIG. 11*b*.

FIG. 11.—Polypoid adenocarcinoma of the colon. *a*, Radiogram of the colon following distension with the barium enema showing no defect; *b*, radiogram following evacuation of barium and insufflation with air. Polypoid growth 4 cm. in diameter, distal loop of the splenic flexure.

examination, prolapse of the rectum and bleeding internal hæmorrhoids were found. Radiologic examination of the colon, by the combined method, revealed a small annular carcinoma at the juncture of the sigmoid flexure and descending colon. This portion of the bowel was resected. The pathologist reported that the lesion was an adenocarcinoma, graded 2 as to malignancy, and that the lymph nodes were not involved.

VAGUE OR TRIVIAL SYMPTOMS

Remaining for consideration are the indefinite, petty abdominal symptoms recited by so many patients. In most instances the complaints have a purely functional basis, but in a small minority they arise from organic disease of the digestive tract which can hardly be discovered without radiologic examination. No consistent rules for distinguishing one group from the other can be offered and decision whether or not the help of the X-ray shall be invoked will depend on the character of the individual clinician's experiences and his intuitive sense of obscure and indefinable tokens of disease. Still another variety of puzzling cases comprises those in which the clinical manifestations are marked, but incongruous, because of extraordinary complications. Here again the X-ray offers valuable service.

An executive of a motor car manufactory, aged 38, came to the Clinic for the annual medical examination required by his company. His history indicated that for several years he had had symptoms typical of peptic ulcer. Of late years he had had little trouble, except for intermittent indefinite distress when his stomach was empty. With the X-ray

a large, perforating malignant ulcer on the posterior wall of the stomach and an ancient duodenal ulcer were demonstrable. At operation no evidence of metastasis from the malignant ulcer was found, and the duodenal ulcer had healed. The pathologist reported that the gastric lesion was an ulcerating carcinoma, measuring 6 by 5 by 2 cm., and was graded 3 as to malignancy. Three years later the patient had gained weight and strength, and was continuing to hold his responsible position.

Until the failure of his bank three months before, a man aged 69 had been in excellent health. He was greatly worried by the bank failure, lost much sleep, and had a peculiar but slight abdominal distress two or three hours after meals. However, he attributed this indigestion to his anxiety. The total gastric acidity was 46, free acids 36. By radiologic examination a minute ulcerating cancer, just below the angle of the stomach, was discovered

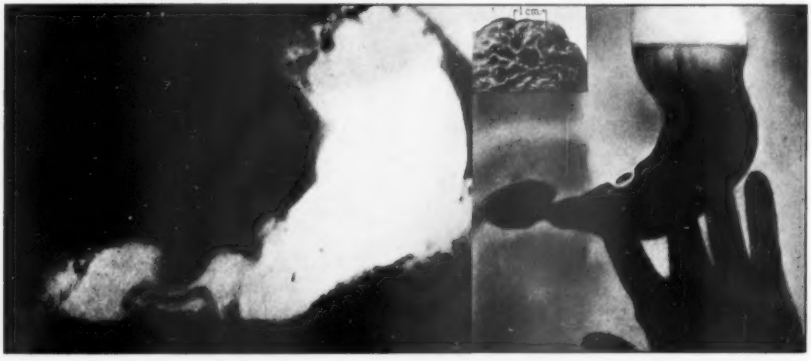


FIG. 12*a*. FIG. 12*b*.

FIG. 12.—Small ulcerating carcinoma of the stomach. *a*, Radiogram of filled stomach showing small defect on lesser curvature below angle of stomach; *b*, drawing of fluoroscopic image with palpating hand exerting pressure to demonstrate typical meniscus-sign complex on the lesser curvature Drawing of specimen. (Inset.)

(fig. 12 *a*, *b*). At operation the surgeon excised the lesion for histologic investigation. The pathologist found that it was an ulcerated adenocarcinoma, 1 cm. in diameter, and graded 3 as to malignancy. Gastric resection, of the Polya type, was then performed.

Occasionally symptoms of disease are pronounced, but are heterogeneous and inconsistent with one another.

For example, a man aged 74 had been well for twenty years, until four months before when he had begun to have abdominal pain with nausea, and had vomited once or twice. His weight had declined 28 pounds (12·7 kg.), and an ovoid, nodular, tender, movable mass, about 5 by 15 cm. in extent, was felt in the right side of the abdomen; the total gastric acidity was 16, and the hæmoglobin was 56%. The radiologist found a minute ulcerating cancer on the lesser curvature of the stomach, and a duodenal ulcer. But neither lesion accounted for the large palpable mass, and after conference with the clinician, who was sceptical of the radiologic data, examination of the colon with the X-ray was agreed upon. This disclosed an intussuscepted tumour of the transverse colon, near the hepatic flexure. Hemicolectomy was performed for the lesion of the colon, an adenocarcinoma, and on exploration the surgeon found the small, ulcerating gastric cancer and the scar of a duodenal ulcer. Following operation, the patient died of complications, and the existence of the gastric and duodenal lesions was confirmed at necropsy and by pathologic examination. The ulcerating cancer of the stomach was 2 cm. in diameter.

In concluding, I do not wish to leave any impression that the signals which I have discussed invariably denote the presence of organic disease, and that the X-ray will invariably find it. Many years ago, someone made the remark that the stomach is

the fire-alarm box of the abdomen. Often the stomach sends out an alarm when the fire is elsewhere or does not exist. Consequently, if the clinician avails himself freely of the X-ray, he must expect to receive many negative reports, often even when the symptoms seem to be pathognomonic. It would be absurd to claim infallibility for the X-ray in the discovery or exclusion of disease, but, if the findings are interpreted competently, it gives worthy assistance in both respects, and I have tried to point out some of the circumstances in which this assistance is likely to prove most valuable.

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Section of Therapeutics and Pharmacology

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The Pharmacology and Therapeutics of Curare and its Constituents

By RANYARD WEST, M.D. (Beit Memorial Fellow)

IN the frequent references to curare in the literature of physiology, from the original descriptions of its action by Claude Bernard (1856) and Kölliker (1856) to recent accounts of its action upon the strength-duration curve of the muscle of the frog, it is exceptional to find mention of the variable composition of the drug or of its variable action. Yet both have long been known. Curare is, in fact, a mixture of watery extracts of a number of poisonous plants. These plants differ in different areas, and are, perhaps, not always the same in any given area. Produced as it is in regions of South America, scattered over many thousand square miles of territory, the best criterion which can be established for curare, either by the standards of Indian hunters, or by those of European physiologists, is that of a powerful poison whose predominant action is the paralysis of voluntary muscles.

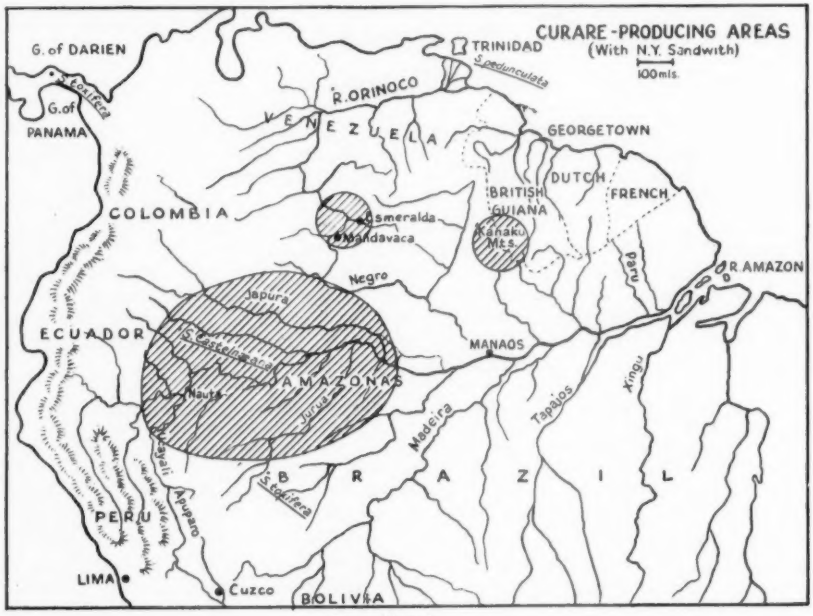
Curare in History: Composition, Pharmacology, Therapeutics

As I have recorded in a previous paper, Sir Walter Raleigh (1595), in his account of the discovery of the "large, rich and beautiful empire of Guiana," refers to curare and its use in war and his desire to find an antidote to its poisonous effects. During the following centuries a number of famous explorers of South America referred to curare in their writings, and Humboldt and Bonplan (1821), on the Orinoco, and the Schomburgk brothers (1844), in British Guiana, saw the poison prepared by evaporation and mixture of plant extracts. It was Humboldt who identified the chief plant ingredient of the curare of the Macusi Indians as a member of the strychnos species, and Sir Robert Schomburgk (1857), who saw it growing, and named it *Strychnos toxifera*. Quelch (1895) compared the ingredients and preparation of curare as described by Waterton (1813), who did not actually see the process at work, and Schomburgk (1844), with his own observations in the same area of the Kanaku Mountains of British Guiana. He found that from six to eight plants entered the brew. The majority of these were poisonous, and in one curare four plants were apparently of the strychnos species. But the constant ingredient he found to be the bark of the ligneous vine, *Strychnos toxifera*. Further westward, on the upper Orinoco, this did not hold true, however, and Robert Schomburgk stated definitely that the curare of Esmeralda, described by Humboldt, did not contain *Strychnos toxifera*, which Schomburgk says was unknown to the natives of that area.

Humboldt was apparently the first to make it clear that there were several different arrowhead poisons used by the Indians of the interior of South America.

He recorded that the curare of Esmeralda on the Orinoco was stronger than that used by the Ticuna Indians of the Amazon. Castelnau saw curare being prepared in Upper Amazonia (Weddell 1851), and it seems probable that the chief strychnos of the curares of these regions is *Strychnos castelnæana*. In another part of the Amazon territory (the Japura river) the strychnos perhaps differ again.

Whilst explorers and botanists were aware of the various and varying ingredients of curare, chemists had succeeded in extracting differing active principles from curares which reached them. The first was curarine. Boussingault and Roulin (1828) obtained a "syrupy body," and a separation by alcohol was made by Pelletier and Petroz (1829). The first preparation in crystalline form was by Preyer (1865). Curine, a second crystalline alkaloid, was first recognized and prepared by Boehm (1896). The latter contributed a standard work on the



MAP I.

chemistry of curare and obtained a 4% to 5% yield of curarine direct from the bark of *Strychnos toxifera* (Cash, 1901).

By the end of the nineteenth century, pharmacologists were becoming aware of varying properties in curare. Tillie (1890) demonstrated a convulsant effect of curarine "after destruction of the anterior brain and exclusion of the legs by vascular ligature." Cash (1901) mentions having seen this effect of curarine, but adds that "two specimens out of three of curare did not show this action, and that "at most curare is but a feeble convulsant and this element of its action is masked by peripheral paralysis." Cash notes that tonic convulsions have been seen in the dog, and he differentiates these from "muscular tremor, which is frequently witnessed in curarized animals." Brunton (1877) suggested that there might be some sensory depression, and Kölliker (1856) and Schiff (1855) each note salivary hypersecretion, though neither of these actions has been generally found. Glycosuria

has been recorded in curare poisoning (Cash 1901). It is important to realize that these earlier observers were aware of varying actions of curare being dependent on different strychnos plant constituents. Curares containing strychnos "curare" were said by Couty and Lacerda (1879) to paralyse the vasomotor mechanism and so cause a profound fall of blood-pressure, while *Strychnos triplinervia* (Amazonia) was thought to be responsible for convulsions.

It may be surprising to us in this country to learn how fully the therapeutics of curare were tried in France in the latter half of last century. The reason given by Cash is the stimulating effect of Claude Bernard's researches. It was used in hydrophobia "to delay the fatal issues"; in tetanus, of which disease Demine treated twenty-two cases with eight recoveries (Busch 1867); in epilepsy, of which large case-series are reported, some writers speaking eulogistically of the drug, though Cash writes that earlier observers were apparently more successful with the remedy than their successors. It was also used in chorea. Probably the dosage employed was usually low. To a case of hydrophobia, Penzoldt (1882) considered that he administered, within two and a half hours, doses which, if given at one time, would have been lethal. But "the power of movement was by no means abolished, for the patient shortly before death sprang out of bed in his delirium." "This," says Cash, "may be regarded as a typical case of the palliative action of curare." Hoche (1894) used Boehm's curarine in a case of tetanus, and Hoffmann had already used the alkaloid in 1879.[1] At the end of the century curare appears to have been considered in France as a recognized therapeutic agent in desperate cases. It was also used, apparently to a less extent, in Germany (Binz 1895, Bergell and Levy 1904). But no attempt appears to have been made to standardize preparations or to obtain curarine in quantity.

There are few references to the therapeutic use of curare in the English literature. Hunter (1878) treated tetanus with preparations of "urali" bark from Appun's (1870) collection of 250 medicinal plants from British Guiana. At the time of the Boer War Messrs. Savory and Moore supplied the drug in brown pellets for use in tetanus cases. During the last thirty years curare appears to have lapsed almost entirely from medical literature, appearing only in the physiological literature of the intimate mechanism of neuromuscular activity.

Properties of Various Curares—the Lissive Action

In 1930 I was given permission, in connexion with an investigation of the mechanism of parathyroid tetany, to administer curare to dogs. The experiment had been suggested to me by Professor Hartridge and we performed it together. The result for which we were looking was obtained when curare removed the violent muscular spasms of tetany. But it was a surprise to find that this could be done in doses which failed to paralyse the animal (Hartridge and West 1931 (a)). Dogs so treated appeared free of their tetany and with full powers of locomotion. Following certain theories of the mechanism of the posture in human tetany, I decided to try the effect of curare on cases of chronic nervous disease with predominant muscular rigidity. Another specimen which had a good rigidity-removing or "lissive" action on dogs in tetany was tried on thirty cases of pyramidal and extrapyramidal rigidity in man (West 1932). The results were irregular and, as such, unsatisfactory, but in the best cases there was a sufficient degree of selective removal of rigidity, as opposed to voluntary power, to make further investigation of curare and its constituents appear justified.[2]

[1] Hoffmann (1879) gave 1 to 9 mgm., Hoche 0·25 to 0·7 mgm. as the dose of curarine.

[2] Sir Robert Schomburgk (1857) indicated what we now call the "lissive" action of curare when he described the paralysis of a horse suffering from tetanus with the drug, and its subjection to artificial respiration, when "it rose up apparently perfectly recovered and eagerly partook of hay and corn."

The question for immediate elucidation was whether this lissive action was a constant feature of curare or occurred only in some specimens. Here I may perhaps refer to the classification of curares. Boehm (1895) placed curares in groups according to their containers, this classification agreeing with his chemical analyses. Curare usually leaves the forest region of its production in one of three vehicles, a small earthenware pot, a hollowed gourd or "calabash," or the interior of a bamboo cane. Boehm described three alkaloids as being present in "pot" curare, a further one in "calabash" curare, and two, different again, in bamboo or "tube" curare. I investigated the actions of several specimens, and the result of their analysis is shown in Table I. The headings of the table have served for a time to differentiate curares pharmacologically. They may be taken in order and their significance described.

TABLE I.—VARYING PROPERTIES OF CURARE

Specimen		Vehicle	Paralysis	Convulsions	Respiratory Selection	Lissive	
						Dog	Man
1	(B.W.)	Unknown	+	0	0	+	
2	(C.S.)	Pot	+	0	0	±	±
3	(G.2.)	Calabash	+	0	0	±	
4	(G.1.)	Calabash	+	0	0	0	
5	(B D.)	Calabash	+	+	+	0	
6	(W.)	Unknown	+	+	+	0	
7	(B.M.)	Bamboo (Ucayali)	+	0	Dog 0 Rat +	±	±
8	(D.)	Calabash (B.G.)	+	0	Rat +		(+)
9	(S.)	Calabash (El Cubo)	+	−	−	(+)	

Paralysis.—Paralysis fulfilling the classical tests upon the frog, which are directed to show an action distal to the motor nerve, is a sine qua non of curare.

Convulsions.—Certain curares show a convulsant action, closely resembling that of strychnine. Convulsions occurred in the frog, rat, and dog, with the use of specimens 5 and 6 in this series.

Respiratory action.—Generally speaking, curare will leave the respiratory mechanism undamaged until a severe degree of paralysis of the limb muscles has occurred. Sometimes, however, certain animals—amongst those I have tried this particularly applies to the rat and mouse—suffer from respiratory embarrassment before there is any sign of weakening of the muscles of the limbs; or else the respiration will suddenly become embarrassed in a partially paralysed animal and will cause its death before the onset of full paralysis. I had come to regard all effects such as this as being due to a separate agent occurring in some curares. But recently I have seen the phenomena in rats under the influence of pure curarine. It is worthy of record that under certain conditions and in certain animals, curarine may have a respiratory action in doses which are inadequate to cause full paralysis and the fact that this action is not always in evidence is one of the reasons for caution in the use of curarine in the human subject.

But there is a further, much more definite, respiratory action, and it is that to which reference is made in Table I.

A dog given a curare of unknown source (No. 6) vomited four minutes subsequently—an unusual event in curare poisoning. After seven minutes his respiration slowed in rate and became laboured. There appeared to be difficulty in inspiration, the breaths being taken very deliberately. A minute later respiration ceased entirely, but the dog was not obviously weakened muscularly, and was standing up at the time. It became cyanosed, but a moment later breathing restarted. There was rapid panting with much salivation and the cyanosis disappeared. After a further minute, slow, laboured respiration recommenced. At this time the front legs were weakened, but there was no general paralysis. During the respiratory attack it was impossible to ventilate the animal by artificial

respiration; it seemed that no air entered the lungs. Immediate tracheotomy showed no signs of obstruction in the larynx. At a subsequent autopsy air entered the pleural cavity with some force, the lungs were very small and appeared rubbery, and no air could be expressed from them. A morbid anatomist described them as appearing "collapsed," but subsequent histological section led to a report of there being no collapse of the lung.

For a time I tried to reconcile such experiences with the selective removal of respiration which sometimes occurs in the rat and in which stimulation through the phrenic nerve may fail before stimulation of the lower limbs through the sciatic. I now incline to the view, however, that while curarine in some animals and under some conditions may affect the respiratory muscles before those of the limbs, the peculiar and dramatic effect which I have just described in dogs is probably due to a bronchial spasm. With one doubtful exception I have only found this action present in curares which contain a convulsant.

"*Lissive*" *action.*—By a "lissive" action is implied, in man, the selective removal of pathological rigidities without apparent diminution of voluntary power. The one sample of "pot" curare in the series (No. 2) is lissive in parathyroid tetany in the dog and in chronic spastic disease in man. In neither is this action always obtained. A bamboo curare (No. 7) and a calabash curare (No. 8) are also lissive, but in rats a selective respiratory action was noticed. It is apparent that the presence or absence of the lissive property cannot be co-ordinated with Boehm's vehicular classification. Further, Specimen No. 1 resembles "pot" (No. 2) and "calabash" (No. 3), though in fact it was believed to be of "tube" origin. It was this curare, obtained from Messrs. Burroughs and Wellcome, with which Hartridge and I first obtained a lissive action in dogs. The convulsant action was obtained from one calabash specimen and one specimen of unknown origin. Neither was lissive to dogs. But two other calabash specimens behaved each of them differently again. No. 3 was lissive, while No. 4 was neither lissive nor convulsant. The table thus shows the classification of curares in terms of their containers to be inadequate to the present research. A collection made by Mr. F. Stevenson on the Ucayali River, and now in the British Museum, contains curares both in pots and bamboo tubes, suggesting that the vehicular classification of curare may not differentiate types even geographically. In this preliminary series, curares which were lissive to dogs in tetany and were tested in human cases, were found to be lissive in them also. But clearly this might not always be the case.

As regards the elucidation of the lissive function of curare, there still remains the alternative possibilities of varying composition and varying conditions of action. Curares vary in composition, but their lissive property runs across the traditional classification, appearing inconstantly in "pot," "calabash" and "tube" varieties. Further, three lissive samples out of four were active at one time and inactive at another. The problem was a confused one.

I decided, in the first place, to collect specimens of curare from as wide an area as possible, to see whether there was any fixed geographical origin for the lissive samples. I found that most of the curare in this country was in small samples in the hands of individuals (who held them as mementoes of travel) or in museums. In many cases their ultimate origin was unknown. I obtained a few ounces of curare as gifts from individuals and a few more ounces of known origin from Kew Gardens and the British Museum. In some cases the quantities were not sufficient for adequate examination. One or two samples proved not to be curare at all, and some unfortunately lost their identity in some preliminary chemical investigations which were undertaken. My aim was to obtain a curare which was at once of known geographical origin, lissive, and in which the lissive factor could be separated chemically. Preliminary chemical separations only could be made with the small quantities obtained at first. But Mr. A. Stephens, at St. Bartholomew's Hospital, worked, first on a mixture of various small samples of curare, and later

on one specimen of calabash curare, and obtained results of considerable interest. Mr. Stevenson's specimen of bamboo curare was the one member of this series in which I found lissive properties and of which sufficient quantities could be obtained for adequate chemical investigation. Samples of calabash curare were brought from abroad by the Medical Research Council and one also was obtained in fair quantity from British Drug Houses. Sir Henry Dale gave me the facilities of his chemical research department, and in this Dr. Harold King worked on these specimens.

Curare Derivatives: Curarine, Convulsants, Central Depressants

Working first on several ounces of mixed curares of various origins, Mr. A. Stephens obtained semi-crystalline curarine of comparatively high toxicity, a resinous impurity of low toxicity but with an apparent central depressant action in frogs, a convulsant alkaloid, and another substance, not an alkaloid, which also caused convulsions in frogs. From the specimen of calabash curare from British Drug Houses he obtained a curarine of high toxicity, and it was with this specimen that I first found curarine to be less effective than some crude curares from the point of view of a lissive action. In addition, he prepared an alkaloid other than curarine which was present in very small amounts and possessed the selective respiratory action which I have described on rats, and a third substance, of which he obtained both a tannate and a phosphotungstate, which was not very toxic, but which appeared to have a central depressant action both on frogs and rats. Neither of these lesser fractions was obtained in quantities large enough to determine the presence or absence of a lissive action in dogs or man. From a calabash curare from El Cubo in Venezuela, in which I had found some lissive action in dogs, Mr. Stephens obtained two convulsant alkaloids, but no lissive fraction (Table II).

From the calabash curare of British Drug Houses Dr. Harold King produced a curarine iodide which had a well-marked selective respiratory action on the dog. This appears to be the one case in which a curarine has shown respiratory selection so strongly as to suggest bronchial spasm as being its method of action. The analysis of the specimen of tube curare, which I obtained in fair quantity by the courtesy of the British Museum, was carried further. Originally it had shown the following properties :—

(1) It was a normal curare, killing by its peripheral action and without convulsions, but with some tendency towards a selective respiratory action in rats.

(2) It was lissive to a moderate degree in dogs in tetany and in human cases of pyramidal and extrapyramidal rigidity. This latter action was inconstant.

From this substance Dr. King isolated pure crystalline tubo-curarine, and I understand this is the first occasion on which this substance has been obtained in crystalline form. In addition, he prepared the second alkaloid curine. The actions of these may be briefly described.

Tubo-curarine in Man

Tubo-curarine killed frogs by the classical action of peripheral paralysis. Subparalytic doses appeared to have a central depressant action to some slight degree, an action which will be described in dealing with curine. On rats, the action was similar, but without trace of central depression. On dogs, there was a purely peripheral action and no trace of lissive power. In man, the drug was given in 5 to 50 mgm. doses to a case of spastic paraplegia from disseminated sclerosis. Doses of *10 mgm.* given subcutaneously caused the following symptoms: The patient complained of slight dizziness within a few minutes of the injection. This was followed by some blurring of vision "as if there were a film over the eyes." There was slight frontal headache and the patient felt hot and "flushed." At this period, from five to thirty minutes after the injection, there was slight ocular ptosis, but

otherwise no sign of motor weakness. The systolic blood-pressure fell slightly, e.g. from 154 to 130—and the diastolic to a less degree—e.g. from 80 to 70. The pulse-rate remained unchanged. The legs, which were in a strong flexion spasm, became slightly less rigid, the right spontaneously adopted a little less flexed posture, and both could be manipulated more easily passively. Walking was not materially improved. With *20 mgm.* the same patient had more giddiness, greater ptosis, a greater fall of blood-pressure (to 118/74) and now a commensurate rise of pulse-rate from 76 to 92. The right leg extended voluntarily with greater ease, and the patient could put this leg to the ground for the first time, but her walking was not improved, because of giddiness. The symptoms and signs persisted definitely for thirty minutes after the injection, but by the end of fifty minutes all these had vanished, including the decreased spasticity. On the following day and until about fifteen hours after the curarine was given the patient was said by the ward sister and by herself to be improved as regards passive but not active movements. Within twenty-four hours she was stiff again. With repeated dosage at the rate of two a week, the giddiness became less annoying to the patient and she remained on the whole less spastic. She seemed to obtain more benefit from massage and physical treatment, and these failed to maintain the improvement when given without tubo-curarine. When the latter was discontinued, spasticity, greater than before treatment, was complained of by this and by other patients. With *50 mgm.*, well-marked symptoms of poisoning appeared. There was almost immediate flushing of the face. In ten minutes ptosis prevented the patient from opening her eyes. She articulated very badly, she could not swallow or raise her head. The arms were weakened but not paralysed, the legs weak and relaxed but not entirely flaccid. The signs lessened after forty-five minutes, the hand-clasp became good again, but it was one hour and fifteen minutes before she could move her facial and tongue muscles readily or raise her head even momentarily. By this time the legs were already stiff again, the position being one of extension, an unusual one for her.

I have dealt somewhat fully with this case, for the results obtained find confirmation and in this patient the essential features of the action of tubo-curarine are present. In small doses it may relax spastic muscles sufficiently to enable physical treatment to be more effective, but essentially it only relaxes spastic muscles as it paralyses them. In this respect its effect is not nearly so good as that of a good sample of crude curare. Its action is more evanescent, and can only be obtained at the threshold of toxic symptoms, which are very unpleasant to the patient.[1]

From the specimen of tube curare which yielded this tubo-curarine, Dr. King obtained two other fractions. The first, which he submitted as a basic lead precipitate differed in no way that I could find from tubo-curarine. It possessed a typical curare action on the frog, but in addition showed signs of central depressant action in small doses. Rats and dogs reacted with no novel incidents, the latter retained their tetany when greatly weakened by the drug. In man the dosage was pushed to cause weakness without the concomitant appearance of a lissive action. The second active principle was curine.

Pharmacology of Curine and Bebeerine

Curine.—During the past year a paper on the chemistry and pharmacology of curine has been published by Hauschild (1934). He records that there is more curine in tube curare than in pot curare, and very little in the calabash variety. In frogs, doses of 10 to 20 mgm. caused a sluggishness of movement. The skin became bright and smooth and there was slight trembling of the muscles. He noted some curare action,

[1] This patient's description of her feelings under the 50 mgm. dose should be recorded, partly because there is here an echo of the suggestion that curare has some sensory action: "I didn't know when I was being touched. I didn't feel the needle. I didn't know you were holding my wrist, it felt like a vice gripping it like ice. When sister put her hand on my forehead I thought it was a lump of ice. In one of my eyes I saw a vision of my little girl very clearly. When you said 'You're all right,' it was my husband's voice that I heard speaking. The skin of my face felt drawn all tight."

and speaks of large doses " paralysing striped muscle like caffeine." Death occurred from heart-failure, with heart-block, a digitalis-like action. In mice Hauschild noted spasms of the limbs, sometimes fatal, and heart-block. Alternatively, death was from respiratory failure. In the cat he studied the cardiac and vascular actions of the drug. He found that curine did not prevent vagus stimulation from being effective, and also that atropine did not affect the action of curine on the heart. He states that curine does not alter the action of acetylcholine on blood-pressure, that it tends itself to lower blood-pressure and that blood-pressure raised by adrenalin is lowered by curine. His conclusion is that curine acts upon the exciting or conducting mechanism of the heart, not through the central nervous system and not upon the vagus terminations. The effect on vascular tone he thought due to impurities.

In my own experiments on the frog I was much struck with the fact that small doses (one-tenth those recorded by Hauschild) produced marked central nervous depression with fibrillary twitches of muscles, and nothing further that I could observe. The frog would lie upon its back or in any posture selected, but when roused (e.g. by an electric current) it would leap with undiminished power across the room. The action was a prolonged one, lasting from half an hour to at least six hours after the injection of 1 to 3 mgm. of curine. It appeared to require ten times this quantity to affect the heart, and at this multiplication of the original dose I noted no electrical signs of a curariform action. As mammals I used very small mice, for I was strictly limited in my supply of curine. They showed sluggishness of movement, appeared sleepy, and at length would remain absolutely stationary. They could, however, be roused to full activity, but only for a moment, after which they relapsed into somnolence. But, in addition, two other features were noteworthy. Tremors, starting in the small muscles of the feet—so that the digits moved spontaneously—spread until the whole body was involved in sudden attacks of tremors amounting almost to convulsions, each lasting for about one second and being followed by an interval of several seconds. During the attacks the eyelids would blink violently and the tail twitch. There was a diminution rather than a rise of reflex excitability. Secondly these large doses produced definite symptoms of weakness of the limb muscles and a strong tendency to kill by a selective respiratory action more marked than had been observed with other curare fractions on rats. After these experiments I was left with 130 mgm. of curine. This was administered to a dog in violent tetany. It failed to relieve the tetany, but it also failed to produce any pharmacological effect. The dose was too small, and with its administration disappeared any present possibility of determining the action of curine upon pathological rigidities.

Bebeerine.—Although we had no more curine, Dr. King drew my attention to a quotation from Spath (1928), that curine is structurally identical with l-bebeerine, an alkaloid of the pariera root, which is accessible on the market. Dr. King accordingly obtained some crude bebeerine and sent me the hydrochloride. Whatever properties the pure alkaloid might possess, this bebeerine which was submitted to me can be dismissed very briefly, though I worked very fully upon it. It has a definite central depressant action on frogs, but this does not kill. Larger doses kill by a curare action, the heart being unaffected. Rats and mice do not show a clear central action, death being due to selective respiratory paralysis. In dogs and man bebeerine has an ordinary curariform action when given in adequate dosage. In neither is it at all lissive, and in one patient the rigidity of a spastic paraplegia was retained when most of the cranial nerves showed paresis. Bebeerine might however be used as a source of a curariform action.

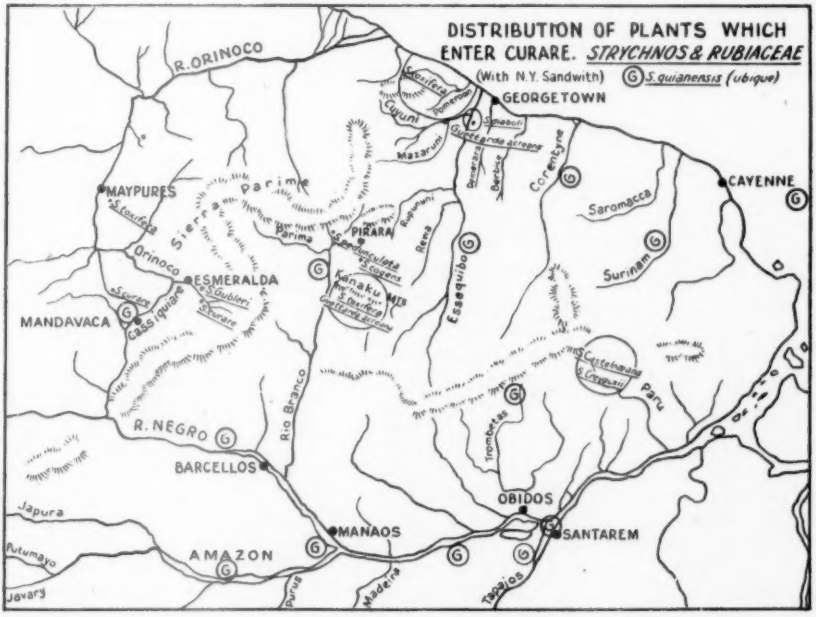
The table summarizes the results to this point. It will be seen that, unless it be curine, which I have not yet been able to give in adequate doses but the isomer of which has far proved valueless, no lissive principle has yet been isolated from curare.

TABLE II.—CURARE DERIVATIVES (1931-1934).

Source	Fractions	Properties	Prep.
Mixed Curares	1. Curarines	1. Curariform (peripheral paralysis)	A.S.
	2. "I" and "XI"	2. Convulsant	"
	3. "K" (resinous) "J"	3. Central depressant (frog)	"
Calabash "A" (convulsant, not lissive)	1. Curarines (picrate and hydrochlor.)	1. Curariform (without resp. selection in rat)	"
	2. Base "R"	2. Curariform (with resp. selection in rat)	"
	3. Phosphotungstate and tannate of unknown base	3. Central depressant (frog and rat)	"
Bamboo "B" (lissive)	1. Basic Pb. ppt. + 2. Tubo-curarine	1. Curariform (with resp. selection in rat); Central depressant (frog)—(with curarization)	H.K.
	3. Curine	2. Central depressant, muscle excitant (frog); Cardiac depressant (frog and cat—Hauschild); Respiratory depressant (mouse)	"; "; "

Sources of Curare Supply

It had become clear that European supplies of curare would not be adequate to solve our problem. I consequently looked to the curare-bearing areas of South America for further supplies of curare itself. At the same time I decided to attempt collection in bulk of some of the known poisonous plant ingredients. Map I, p. 42, shows the chief areas in South America in which curare is known to have been



MAP II.

produced. Inquiries satisfied me that the most likely sources of good curare were the upper Amazon basin and British Guiana. I knew that tube, calabash, and pot curare could be obtained from the former area, while calabash, and possibly pot curare could be got from British Guiana. I could not say which curare I required and I approached both areas. In the case of Amazonia, the only approaches possible were

by special expeditions or through individual channels. I have not yet received recently collected curare or plants from these regions. Professor Ducke of Rio de Janeiro has given me a great deal of botanical information however, and a number of strychnos seeds have been sent by him to Kew for germination. He will look for further material in his forthcoming expedition this year.

British Guiana offered better facilities in view of the organization of the Colony and its administrative link with London. I obtained valuable information from missionaries and approached balata traders, botanists and government departments. Dr. Roth, the late Curator of the Georgetown Museum, and a great authority on native arts, crafts and customs, thought curare could be obtained in quantity, and negotiated with a traveller to the interior to this end. Only small quantities were forthcoming, however, for the Indians use the poison much less than formerly. With introductions from Sir Arthur Hill, the director of the Royal Botanical Gardens at Kew, and with the support of Sir Walter Fletcher, the secretary of the Medical Research Council, I secured the collaboration of the Forestry Department in Georgetown, and Mr. Wood, the chief officer of the district sent an expedition into the interior on my behalf. His colleague, Mr. T. A. W. Davis, sent ample supplies of the bark of six plants of the Strychnos species and a poisonous plant of the Rubiaceæ. These samples were identified at Kew by Mr. N. Y. Sandwith, who has dealt with their botanical significance in recent publications (1933) and to whom I am indebted for the botanical information in the following tables. The materials were then handed to Sir Henry Dale at the National Institute for Medical Research, where their chemical nature was investigated by Dr. Harold King.

Strychnos Plants from British Guiana

TABLE III.—INGREDIENTS OF CURARE (TRADITIONAL)

In British Guiana	*In Upper Amazonia*
S. toxifera (Kanaku Mts.-Macusi curare)	*S. syntoxica* (Venezuela-Cunipusana curare)
S. cogens (i) Pirara-Macusi curare	*S. triplinervia*
(ii) Esmeralda "Cumarawa")	
	S. Castelnæana (Ucayali-Ticuna curare)
S. pedunculata ("Devil-doer"-"Yakki") (Pirara-Macusi curare)	
Guettarda Aereana (Apoteri.) ("Yakki"-Macusi curare)	

Table III shows the poisonous plants believed by tradition and by the accounts of travellers to enter into the composition of curares in the two areas of British Guiana and Upper Amazonia. Two strychnos plants in one area are closely allied botanically with two in the other and these I have placed beside each other—*toxifera* and *syntoxica* on the one hand and *cogens* and *triplinervia* on the other. The map shows where the different plants which are believed to be active ingredients of curare have been located up to 1932. The areas visited by Mr. Davis are shown with a cross. *S. cogens* he did not find; it has not been seen for many years. It is a traditional ingredient both of Macusi curare and of the "cumarawa" of Esmeralda, and its rediscovery would be of great interest alike to the botanist and to the pharmacologist. Mr. Davis writes that it probably still grows in the Pakaraima and Kanaku Mountains, and possibly further west in Brazil. To find it would require a special journey of perhaps several months, and one hesitates to ask for this until all the more accessible species have been examined. *S. pedunculata* also is very rare; herbarium specimens only were obtained. Table IV shows the species which I received, their source, the quantity of alkaloid, and the pharmacological action. In two, *S. Mitscherlichii* and *S. Melinoniana* there was little or no alkaloid and no pharmacological action in the quantities available. *S. Erichsonii* had a strychnine-like convulsant action. Its presence would account for the convulsant action of

TABLE IV.—POISONOUS PLANTS FROM A "CURARE" AREA OF BRITISH GUIANA.

Specimen (Sandwith)	Source (Davis)	Historical note	Alkaloids (King)	Pharmacological action
S. Melinoniana	Pomeroon River		+	
S. Erichsonii	Pomeroon River		+ + +	A convulsant resembling strychnine
S. Mitscherlichii	Pomeroon River		0	
S. diaboli, Sandwith	Essequibo R. (Sandwith) Mazaruni Sta. (Davis)	"Black devil-doer"	+	(1) Central depressant (frog, dog) (2) Weak peripheral action (3) Lissive (tetany dog)
S. toxifera	Pomeroon River	Macusi Curare (Schomburgk)	+ +	(1) Peripheral paralysis (2) Slightly lissive
Guettarda Acreana	Apoteri Rupununi River	"Yakki of Macusi Curare	+ + +	Central depressant (frog)

some curares and for the convulsant isolated from calabash curare by Mr. Stephens. Of the two species traditionally associated with a famous curare—that of the Macusi Indians—*Guettarda Acreana*, though rich in alkaloid, had only a mild central depressant action in frogs and no action at all when given to dogs in fairly large doses. Perhaps it may be possible to do further work upon this plant in view of its high alkaloidal content. From only one of these plants has the alkaloid yet been isolated, and that is the strychnos from which curarine has been prepared in the past, *S. toxifera*.

Strychnos toxifera—Curarine

The crude extracts of *S. toxifera* had shown a curariform action, without central depression or convulsions appearing. There had, however, been some slight lissive action. The extracts were less effective in this respect than good crude curare. The action of the crystalline curarine chloride prepared by Dr. King need not be described at length. Essentially it acts like the tubo-curarine already described, only points of difference require mention. In the first place, from the samples submitted to me, curarine appears stronger in its action than tubo-curarine. In man doses of *5 to 15 mgm.* produce symptoms of weakness of cranial nerves. Secondly, there is less tendency for the blood-pressure to fall. The lissive effect of the crude extracts on dogs in tetany is not shown by pure curarine, and in cases of Parkinsonism or of spastic paraplegia there is no margin between the dose which will lessen rigidity and that which causes weakness.

The only advance then, with regard to curarine, is that it can be obtained in quantities which render it less precious than all the substances connected with curare have hitherto been. For *S. toxifera* is a species which is widespread in tropical America, and its yield of curarine is good. I think the therapeutic uses of curarine will remain very limited. In 1932 I reported that I had not had an opportunity of treating a case of tetanus with curare. Since then I have seen one case, a severe and fatal one occurring in a woman of 48, five days after infection. It was at a time when my supplies of curarine were still very small, and I used a crude curare which was not a good lissive specimen. It was not possible to control the attacks without giving paralysing doses of the drug, and though a Drinker respirator was introduced the patient died of tetanus with symptoms of hypostatic pneumonia—a danger which may be enhanced by curare. Dr. Leslie Cole (1934), using a curare which he kindly allowed me to test, and which had a moderately lissive action in dogs, treated and reported two cases in which he was more fortunate. In neither did he give paralysing doses, yet in both he considered that he relieved the tetanus spasm. Professor Florey (1934), who recently received some of our curarine for trial in experimental tetanus in animals, found it necessary to give paralysing doses to obtain beneficial results. I am anxious to treat

further cases of tetanus with curarine, because controlled paralysis with artificial respiration offers, in my judgment, at least a more hopeful means of establishing a standard treatment for severe tetanus than the use of curares of variable strengths and lissive powers which have been tried and despaired of for more than half a century.

Strychnos diaboli

One strychnos in the last table remains. *S. diaboli*, collected by Sandwith on the Essequibo River in 1929, was found by Dr. King to be poor in alkaloidal content. Its Indian name has however been translated "black devil-doer," which suggests perhaps that either the name is wrong and a species closely resembling it is highly poisonous, or that the active principle is chiefly to be found in parts of the plant other than the bark which came to us. The fruit is as yet unknown. The crude extracts originally sent to me were strong enough to give interesting results which have been repeatedly confirmed with subsequent more concentrated solutions. *S. diaboli* contains a centrally acting nervous depressant. In the frog this has an action more pronounced than that of any other substance I have described in this paper. Under its influence frogs, quite capable of full activity on stimulation, will lie on their backs inert for hours. They can be killed by the extracts without peripheral paralysis occurring, though the latter can be demonstrated with large doses. Rats are made sleepy by the extracts, though they are ultimately seized with respiratory distress, become cyanosed, struggle and die by respiratory failure. Dogs stand large quantities of these weak extracts (the equivalent quantity of active principle is of course unknown). I have not obtained signs of central depression in a healthy dog. But I have repeatedly removed violent tonic and clonic parathyroid tetany with doses which have no effect on the normal dog. Typically tetany is removed in thirty to forty-five minutes and remains absent for from twelve to eighteen hours. Beyond a nervous action, which may be either central or peripheral, the only probable agency for such an effect, would, I think, be a rise in the calcium content of the blood. Repeated experiments showed no rise in

TABLE V.—STRYCHNOS DIABOLI AND CURINE

	Frog		*Rat*		*Dog*
	Central Depression	Peripheral Paralysis	Central Depression	Peripheral Paralysis	Lissive (tetany)
S. diaboli (crude)	++	(+)	+	Resp.	+
(Hg. Cl_2 ppt.)	+	+	?	+ (Resp. +)	
Curine	+	(+)	+	Resp.	?

serum calcium to take place. Quantities did not permit of dosage likely to be effective from being reached in man. But in view of the results in the dog, further supplies are being obtained, and Dr. King is attempting to isolate an active principle from them. Table V shows my results with *S. diaboli* so far. There is a somewhat striking similarity with the action of curine, though I have not seen muscle fibrillation with *S. diaboli*.

Summary and Review

In this paper I have tried to present the present problem of the pharmacology and therapeutics of curare as it has appeared to me during the past two or three years. I hope I have succeeded in showing that this substance is variable in its plant ingredients, in its pharmacological properties and in its therapeutic value. We should, perhaps, speak of the curares, rather than curare; and of the curares those of three great areas have been differentiated—the curares of Upper Amazonia, of the Upper Orinoco and of British Guiana. Into some of the first probably enters *S. castelnæana*, into the second *S. cogens* or *S. gubleri* or both. These strychnos plants may be responsible in each case for the paralysing action of the drug, a

function equivalent to that of *S. toxifera* in the curares of British Guiana. But of five different strychnos from the Guiana area, one paralyses, one convulses, one is primarily a central nervous depressant, and two appear to be non-toxic. *Whenever two or more different strychnos enter a curare, the possibility of one of these possessing an action other than curariform is thus to be considered.* The varying degrees of usefulness in curares supported such a view, and it was to extract a therapeutic weapon from its lethal and almost useless neighbours that this research was undertaken. It would be a disappointment if curarine in quantity for the treatment of desperate cases of tetanus were its only outcome.

The nature of curarization is not discussed in the present paper. But we have curarine for research as well as for therapeutics. Florey, Harding and Fildes (1934) in their investigation of experimental animal tetanus have already confirmed my finding that curarine itself is not "lissive"—it shows no power of the selective removal of pathological rigidity under the conditions in which we have used it. It is, I suppose, not impossible that its use might throw light on some of the controversial aspects of the physiology of the excitability of muscle through its motor nerve. It would certainly be of great interest to know whether the selective actions of curare on decerebrate rigidity described by Bremer (1929) and his colleagues holds good with curarine. Similarly will it be of importance to know if curarine reproduces the selective action of small doses of curare on the response of the muscle to certain strengths and frequencies of stimulation through its nerve of supply, as recorded by Briscoe (1934). In the results of some of these experiments we may find a further justification for searching for the various active ingredients of curares, and an indication, if this should be the case, of a second substance acting peripherally.

Behind the curares lie the strychnos of tropical America. By searches such as we are making we are opening up the pharmacology of these species, so many of which appear to be poisonous, beyond the starting points of *nux vomica* and *toxifera*. It is little more than a century since India yielded strychnine and brucine. In Africa, forest officers are constantly adding to the known strychnos of various parts of the continent. Some wider systematic survey of the pharmacology of these species may soon be called for. In the research to which this paper is a contribution it is the poisonous plants—especially the strychnos, of curare-bearing areas of South America that engage our attention, and I may end this paper suitably with two relevant quotations. One, from Humboldt: "A fine chemical and physiological investigation remains to be accomplished on the toxiques of the New World"; and the other, Sir Robert Schomburgk's comment: "Unfortunately but little advance has since been made in that direction and the same important desideratum remains still to be accomplished." That was eighty years ago, and to-day we are but starting to till a field which I hope may yet prove as fruitful as those two great scientific explorers anticipated.

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Section of Urology

President—J. B. MACALPINE, F.R.C.S.

[*November* 22, 1934]

Transposition of Right Kidney as a Result of a Perinephric Hæmatoma.—H. P. WINSBURY-WHITE, F.R.C.S.

The patient, a man, aged 67, was quite well until one year before admission for operation when he fell and fractured several ribs on the right side. His complaint was pain in the right side ever since his accident.

Ten months after his fall, a plain skiagram showed a faint rounded opacity extending across the right lumbar region, while on the outer margin of this shadow there was a somewhat vertical opacity about one inch broad and three inches long. The urine at this time contained no pathological elements and cystoscopy showed good functional activity of both kidneys. No swelling could be felt in the right lumbar region.

One week after the plain skiagram, an intravenous urogram was carried out. This showed both kidneys to be functioning well and in their proper position, and the swelling in the right lumbar region to be to the outer side of the right kidney. No operation was advised because of the uncertainty of the condition.

Nine weeks later the patient's doctor wrote to say that there was now a large palpable swelling in the right loin. On the patient's readmission to hospital a large cystic swelling was found occupying the greater part of the right side of the abdomen. Ascending pyelograms were carried out on both sides and examination revealed the fact that the right kidney was now lying well to the left of the vertebral column, while the right side of the abdomen was occupied by a large mass which caused a shadow on the film. The upper two-thirds of the right ureter and the pelvis of the right kidney lay along the left lateral margin of this opacity. The ascending pyelogram of the left kidney showed it to be in its normal position, the right kidney lying apparently superficial to it.

At operation through an incision in the right loin, eight pints of blood-stained serous fluid were evacuated. A huge sac lined with granulation tissue and extending across the middle line was noted. It was impossible to feel the kidney or to identify any other organ. On examining the wall of the sac formed by the overlying ribs, several semi-detached fragments of bone, obviously resulting from injury to the ribs, were identified and removed. The sac was drained and ten weeks after the operation there was still a portion of the cavity which had yet to heal.

Calculi in the Renal Tubules.—R. H. O. B. ROBINSON, F.R.C.S.

This case is of extreme interest because of the unusual distribution of the calculi.

The patient, a woman, aged 44, came to St. Thomas's Hospital in January 1934, with a three months' history of dragging pain in the left loin. X-rays showed an irregular shadow in the left lumbar region. Cystoscopy revealed no abnormality, and the urine was normal. Pyelography showed the shadow to be in the lower pole of the kidney outside the calyx, and without dilatation of the calyces (figs. 1 and 2).

Nine months later the patient returned still complaining of pain, and it was decided to explore the kidney. Perinephritis was present, particularly marked over the area involved, at which point the cortex was slightly depressed, gritty, and

yellowish in colour. The rest of the kidney, pelvis, and ureter appeared normal. The kidney was removed, on the supposition that the condition might be tuberculous. Macroscopically, there was a wedge-shaped area containing small calculi embedded

FIG. 1.

FIG. 2.

in the renal tissue and firmly adherent. Microscopical sections showed chronic fibrosis of the kidney with dilatation of the tubules in the region of the calculi, the tubules being full of calculi. A section of the wall of the renal pelvis showed evidence of chronic inflammation (fig. 3).

Previous to the operation the patient had been taking a normal mixed diet, and had not had any excess of alkalies. There was no evidence of disorder of the

FIG. 3.—Showing one large calculus and other smaller calculi lying in dilated tubules.

parathyroid glands, the plasma phosphate being 2·4 mgm.%, and the serum calcium 10·2 mgm.

Winsbury-White has recorded a case of calculi in the renal tissue, but in this case the stones were lying loose in a cavity in the kidney substance.

Kidney Removed from a "Typhoid Carrier."—W. E. UNDERWOOD, F.R.C.S.

The patient, a soldier, had been invalided home as being a carrier of typhoid; a complete examination revealed nothing, except that the urine on cultivation grew a pure growth of *B. typhosus*, but contained only a few pus cells. Cystoscopy showed a normal bladder and normal ureteric orifices.

Ureteric catheterization.—Right: Clear urine; sterile. Left: Pure growth of *B. typhosus*. Intravenous pyelography showed a normal pelvis on the right side, but no secretion on the left. Instrumental pyelography showed a large hydronephrosis on the left side holding 60 c.c. Left nephro-ureterectomy was carried out. Microscopic examination of the kidney showed no abnormality. The pelvis showed pyelitis cystica.

The patient made an uninterrupted recovery. His urine had been cultivated twenty times during the last four months. It remains sterile and contains no abnormal cells.

A Ureterocele which presented at the External Urinary Meatus (Female).—J. B. MACALPINE, F.R.C.S., (President).

A married woman, aged 32, stated that she had suffered from vesical irritability from childhood, and at about the age of 12 noticed the onset of intermittent and quite transitory obstruction. At the age of 29 she became pregnant, and after the first month or two suffered severely from urinary obstruction. It was accompanied by right-sided renal colic. At a later period in the pregnancy a lump presented at the external urinary meatus and ultimately developed to the size of a cherry. Bladder

obstruction and renal colic were always present when it appeared. It was possible to replace it, when the obstruction would be relieved.

Cystoscopy showed a large object which rose steeply from the position of the right ureter and towered above the cystoscope. Its upper extremity was difficult to visualize. An attempt at per-urethral destruction was not immediately successful, and the patient being rather temperamental, the ureterocele was removed by suprapubic operation which is probably the most satisfactory method for so large a ureterocele. When fresh, this specimen was about 3¼ in. in length. The portion which presented externally is much engorged and of a deep plum colour, the remainder of the cyst having the appearance of healthy bladder mucous membrane.

Large Concentrically Laminated Fibrinous Balls unattached in the Bladder.—F. PARKES WEBER, M.D.

An account of the case from which this specimen (shown at the meeting) was taken is published in full in the *Journal of Pathology and Bacteriology*, 1935, xl, 351-355.

[*January* 24, 1935]

DISCUSSION ON THE TREATMENT OF URETERIC CALCULI

OPENING PAPERS

I. Mr. Henry Wade

SOME little time ago there came under my care a cripple, a woman aged 45, with a hip-joint ankylosed in the position of extreme adduction, from healed tuberculous disease. She was treated by operation (sub-trochanteric osteotomy) after which the limb was put up in abduction.

For several weeks she was an inmate of my wards and after a further stay in a Convalescent Home she returned to her native village. She had only been home a few weeks when she developed complete anuria from no apparent cause, so much so that her doctor thought it was possibly hysterical. From the Monday to the Saturday she did not void a single drop of urine, but apart from this her health appeared to be satisfactory.

On the Saturday morning she was again admitted under my care. She was conscious; her intelligence was clear, but she was somewhat drowsy. The blood urea stood at 160 mgm. %. An X-ray examination was made and when the wet plate was examined the diagnosis was clear and the treatment indicated obvious. The faint outline of a left kidney—which had been destroyed—with an impacted ureteral calculus beneath it, was apparent and a right kidney was shown with multiple calculi, one of which was blocking the outlet from the pelvis.

Under gas-and-oxygen anæsthesia she was immediately operated on; the right kidney was cut down upon, the stone removed, and the concretion blocking the outflow channel taken away. Active secretion was at once resumed and she recovered after a speedy convalescence.

There are several interesting points in this case. The first is the fact that never from her history or from the ordinary methods of side-room examination were her kidneys suspected to be otherwise than in perfect health during the months she was under our care. She never had colic, never pyuria; by no sign or symptom was the presence of the stones revealed. Still, a silent ureteral calculus appeared at one

time to have destroyed completely the functioning power of the left organ and a calculus being displaced into the right channel produced calculus-anuria. Another point is: Were we at fault in failing to have a complete urological examination made when she was admitted with an orthopædic deformity? The answer to that question depends entirely on the school of thought to which you belong. Personally, I make no apology for the course we followed, and would do the same again.

Margaret C., at the age of 4, came to me with a stone impacted in the right ureter at the pelvic brim. Operative treatment was carried out and the stone removed. Convalescence was normal and the result appeared to be satisfactory. She grew up, went through her schooldays, taking part in the vigorous exercises that schoolgirls now enjoy, with no complaint except a very occasional touch of hæmaturia. At the age of 17, she came back under my care. Investigations showed a right kidney that was really dead—a functionless organ which I removed. The channel was not occluded. The kidney was not the site of any pyogenic or other infection. In my opinion, it was at the age of 4 that the irreparable damage had been done.

The presence of the stone has to be confirmed first and thereafter the degree of damage, if any, has to be determined. The methods at the disposal of the urologist are now so accurate and exact as to be almost infallible. There are, however, several pitfalls.

A calcareous gland producing extra-ureteric pressure and consequent narrowing of the channel may be mistaken for a concretion within the lumen.

Many years ago I was examining a student clinically and, as we stood by the bedside, our attention was directed to a young lad in the neighbouring bed who turned groaning on his side and presented all the characteristic appearances of an attack of acute renal colic on the right side. So typical was the attack and so characteristic the small concretion that was taken to be in the abdominal ureter, that several days later I operated on this patient. The right ureter was exposed extraperitoneally. It was observed to be dilated down to a point above the pelvic brim; here it suddenly became narrowed in its lumen, not due to any stone that could be felt within the channel. On opening the peritoneum, however, there was revealed, adherent to its anterior surface, a small calcareous mesenteric gland, the site of healed tuberculous disease. This was removed and a cure was thereby effected.

Phleboliths in the pelvis constitute the *pons asinorum* of the junior student of urology. Their situation, their contour, their size and density, their multiplicity are all points that enable us to recognize their nature and differentiate them from calculi within the lumen of the ureter. But sometimes an element of doubt exists, and this is only cleared up by the passage of an X-ray ureteral catheter which, by outlining the course of the ureter, demonstrates that the concretion is situated some distance from that channel. At first sight, this means of diagnosis would appear to be free from all possible error, but, sometimes, although a single ureteral orifice is observed and the assumption is that a single channel extends from there up to the kidney above, the ureter may have divided just above its entrance into the bladder and two channels be thus formed. In one of these channels a stone may lie and the other, allowing the passage of the X-ray catheter, may lead to the assumption that the shadow seen some distance from it is not within the lumen of a ureteral channel.

At the back of the mind of many of us there is always the question arising: Is it possible that a ureteral calculus may be present within the channel and, from its chemical nature, fail to be demonstrated by a well-taken X-ray photograph? According to the chemistry of certain stones, this should be a not unusual experience. On looking back over a number of years, in which I have dealt with many such cases, I cannot remember a single one in which we failed to demonstrate a stone when it was present, or in which a second examination revealed our mistake, or a friend or

colleague told us of our error, nor one in which the patient voided the stone after we had given a negative report. In other words, it is the oxalate stone with which the surgeon has to deal; all others do not matter clinically—except, in my experience, the cystine stone.

In this latter connexion, I can claim a somewhat unusual experience, in a family in which for some generations intermarriage has been the custom. Many members of this family have suffered from cystinuria and personally I have had to do with five of them, particularly with three cousins, each having cystine stone in kidneys, ureters, and bladder. In two the examination was simple and the stone easily revealed, but in one, although the photograph was equally well taken, the stone was only outlined by a negative shadow, after the introduction of an opaque medium and the subsequent taking of a ureterogram.

The estimation of the degree of damage produced by the presence of ureteral calculi.—The most obvious clinical indication of the presence of a ureteral calculus is when it gives rise to an attack of acute colic, in consequence of the obstruction to the outflow of urine that it produces, the backward pressure thus caused leading to to overdistension of the urinary reservoir above. Fortunately, however, this is usually transient, and, in the great majority of cases, the stone is voided naturally without causing any permanent injury to the kidneys or urinary passages.

On the other hand, a stone may lead to the silent death of a kidney, a process carried out in a painless and unconscious manner. It is therefore important to employ accurate means to determine the damage that has resulted. By *infusion urography*, it may be demonstrated that above the site of the obstruction the ureter and renal pelvis are markedly dilated—an observation of value. I attach more importance, however, to examination by *chromo-cystoscopy*, whereby the expulsion of the coloured urine, instead of taking place by the explosive ejaculations that normally are observed on the healthy side, is first of all delayed in its time of appearance, and, secondly, when it does occur is emitted in a slow rising column, like a smoke signal.

There is now, however, a still more valuable method of examination for these cases and that is *excretion urography*, a vital test of physiological function, better than any we have yet used. By means of it we can estimate accurately the function of the damaged kidney and the extent of the harm that has been produced.

The treatment of ureteral calculi may be considered under four headings: (1) Cases in which the calculi undergo natural expulsion; (2) cases in which natural expulsion is facilitated and expedited by suitable medical treatment; (3) cases in which expulsion is facilitated by trans-urethral instrumentation; and, lastly, (4) cases in which open operative treatment can be employed best. I am electing to deal with the last.

The problem is when to interfere surgically. The time factor is undoubtedly of importance. The ureteral calculus may be producing little, if any, harm. It may be of the type that I would call "bouncing stones," coming down to a slight stricture in the ureter and going up and down from there, so that after repeated X-ray examinations carried out over many months little change is shown to have taken place. Such a case I think can be well dealt with surgically. Where a ureteral calculus has been located in a certain situation, such as outside the wall of the bladder at the lower end of the pelvic ureter, and despite repeated attacks of renal colic and suitable treatment, it remains firmly immobilized in that situation, here, especially if any damage has resulted from its presence, operative treatment should be carried out. The size of the stone, its nature, and the degree of obstruction it is producing are all factors that influence our decision, but each case has to be judged on its merits. The experience of the surgeon will be a factor of influence, and I frankly acknowledge that personally I like the knife. It is so certain, so safe, and so simple.

When considering the operative treatment of ureteric calculi, we may disregard

those cases in which an impacted ureteral calculus has done such serious damage to the ureter and kidney above, by persistent backward pressure and frequently associated infection, as to necessitate the performance of the operation of nephrectomy and ureterectomy. Again we need not consider at length those cases where primary ureteral calculi form in the ureter, the site of an achalasia at the uretero-vesical junction. I would rather dwell upon those cases in which the removal of the stone in itself will be sufficient to effect a complete cure.

In my experience a stone impacted at the uretero-pelvic junction can best be treated by pyelotomy carried out after the exposure of the kidney and by means of the customary technique.

When a stone is situated from 5 to 10 cm. below the uretero-pelvic junction, its removal may be carried out speedily and in a simple and safe manner through a grid-iron incision in the loin, dividing the muscles in the direction of their fibres—an extra-peritoneal removal. If this operation is proposed, however, I would remind you that the channel above the site of impaction will be dilated and therefore, although the stone cannot descend, it can readily slip up into the renal pelvis, and if it does so a more elaborate operation necessitating the exposure of the kidney will probably be required, a procedure which can readily be avoided if the ureter is sought for first at its upper end. When found here, a tape is put round it and on this the assistant exercises gentle traction, so that no stone can slip past it. The assistant has the responsibility of preventing the escape of the stone. Similarly the stone occasionally found impacted at the pelvic brim can be simply removed through a grid-iron incision.

The cases that call for greater skill are those in which the stone is impacted in the pelvic ureter in the usual situation just outside the wall of the bladder. Many surgeons in dealing with such cases, prefer to take the para-vesical route. Personally, I much prefer the iliac approach by the extra-peritoneal route. If this operation is to be done delicately and skilfully, I find it is preferable to do it under spinal anæsthesia with the complete relaxation that is thus afforded. The usual incision parallel to the outer portion of the inguinal ligament is made, the muscles are divided in a line parallel to the original incision and the transversalis fascia is exposed. It is particularly important that this be divided, otherwise a little difficulty may be experienced in finding the ureter. By sight and by touch the ureter is located as it passes over the pelvic brim and is here isolated along with the para-ureteral tissue. A tape is put round it and gentle traction exercised on it. The ureter is now defined by finger dissection down into the pelvis, care being taken to avoid damaging the ureteral vessels that join it at right angles to its long axis. Below each of these a tape is inserted until the lower end of the ureter is reached and the stone palpated. If it can be milked backwards, I consider it preferable to remove it by opening the ureter just above the pelvic brim. If it is impacted and can be felt and seen, it is removed by incising the ureter over it and extracting the stone. The wound in the ureter is then closed by the finest catgut, the stitches passing through the adventitia, and the wound is closed after a small rubber dam drain has been inserted. These wounds heal in virtually all cases by primary union without any leakage of urine, and the results are most satisfactory. It is important to remember, however, that this technique is not suitable for a case where the ureter has previously been exposed as the pelvic peritoneum is more adherent and is liable to be torn.

Where the stone is impacted deep in the wall of the bladder and cannot be seen, is felt deep in the tissues, I strongly advise that it be not approached by opening the ureter, but that the bladder be opened suprapubically, the ureteral orifice on that side viewed, the stone located by a delicate probe, the ureter slit up from where it enters the bladder and the stone extracted. It may appear that this is an unnecessarily elaborate technique for such a case and that a primary

transvesical route in such cases would have been preferable. In some that is true, but in others such a method may lead to difficulty if not to disaster. With the lower end of the ureter first exposed and a finger behind the stone, its exact location by the transvesical route I have described is then easy. Where such a guide is not present and a blind search is carried out, the stone may be found only with difficulty and serious damage may be done to the lower end of the channel in the course of the search. Where the ureter and renal pelvis are found to be markedly dilated as the result of the obstruction, it might at first sight appear advisable to drain these channels and thus reduce the distension. I strongly advise that this be *not* done as it is very liable to be followed by infection. If the wound in the ureter is closed and the channel beneath is free and unobstructed, the dilatation of the ureter and renal pelvis may be expected to subside in a natural manner.

II. Mr. J. G. Yates Bell

The majority of ureteric stones are passed naturally, but this number would be greatly increased if one could wait for some months. To quote Braasch :—

> "In all probability the majority of stones in the ureter pass spontaneously ; while no rule can be adopted, it would be rational in the majority of cases to wait at least two or three months, until Nature has made several attempts to dislodge the stone. On the other hand, repeated violent colic, the danger of renal destruction and other complications as a result of the obstructing stone may necessitate its removal before this period has elapsed."

I would say that—in addition to renal damage by obstruction—infection, pain, and economic reasons call for interference. The patient cannot afford to be laid up for so long with recurring attacks of pain.

Transvesical manipulations have an important part to play in hastening the normal process and will many times do away with the need for further operative interference. But there is no rivalry between these methods and open operation ; they are supplementary, and operation may have to be carried out after failure of manipulations.

General considerations.—Cystoscopy should be carried out in all cases. It gives information as to the size of the ureteric openings, and of infection if present. One must look out carefully for an efflux to see whether there is complete renal retention. The size of the lumen of the ureter is ascertained by a catheter and injected opaque fluids. Dourmashkin says this is dangerous, because irritating dyes may be retained. It is usually advisable to carry out an intravenous pyelography as well ; much information is gained by this means, and some idea of renal function is obtained.

As a result of these investigations, the relative size of the stone and the ureter below are known. This is important, for recently I had a case of a very small stone (the size of an apple-pip) at the sacro-iliac joint but even after ureteric meatotomy, the ureter would admit a No. 9, but not a No. 12, ureteric catheter ; three inches of ureter were congenitally narrow, and necessitated removal by open operation. Children are able to pass relatively very large stones.

The situation of the stone is important, the best results being obtained from manipulations when the obstruction is at, or below, the sacro-iliac joint. When a stone is still above this level after two attacks of colic, only rarely are cases of manipulation successful, the method with several catheters being the best for this type. This is because of the three definitely narrow areas at the uretero-pelvic juncture, sacro-iliac joint and the intramural portion.

The progress of the stone should be watched weekly under X-rays and careful observations should be made on its size.

I will now mention the contra-indications, as manipulations may be said to be worthy of trial in the great majority of cases.

Renal infection as shown by high temperature, renal retention for more than ten days, and increase in size of stone during period of observation, are absolute indications for open operation and therefore contra-indications for manipulation. Poor renal function with a stone in the better side, even without renal retention is a contra-indication, as the œdema resulting from the manipulation may cause anuria.

Principles employed.—The stone is obviously held up, therefore the ureter must be dilated below; to do this adequately in most cases it is necessary to incise the ureteric meatus. If the long axis of the stone is not in the line of the ureter, attempts must be made to bring this about by bougie manipulation, and, rarely, one may pass on to bring down the stone. It should be remembered that the stone will often need to be crushed on its arrival in the bladder, particularly in males. Also, with a view to prevention of recurrence, the fragments must be analysed and a suitable diet and medical treatment arranged.

Methods.—A spinal anæsthetic and open ether are both satisfactory. Dilatation of the uterer is usually carried out by the passage of gum elastic bougies through an operating cystoscope. Another method is to pass two or three ureteric catheters and to leave them in situ for from twenty-four to forty-eight hours. This has the advantage of draining away stagnant, and possibly infected, urine, and in some instances the stone has been withdrawn with the catheters. It has the disadvantage that it can be used for only very small stones.

Swift Joly and Dourmashkin use an inflatable rubber bag over the eye of a ureteric catheter which is introduced and distended below the stone, and have had good results. The method seems reasonable if one can only be certain of the bag not bursting.

Rotation of the axis of the stone is done by a bougie and explains itself. X-ray examination is necessary to verify the change.

Incision of the ureteric meatus and intramural portion of the ureter is the most important step and, in my opinion, should be done always with an irrigating operating cystoscope, otherwise bleeding may give trouble. The scissors used are well-known and an accurate cut can be made with the blunt-ended blade in the lumen, but several cases of severe bleeding undoubtedly have occurred. I have had one myself, in which, after three days, a second cystoscopy had to be carried out with an irrigating cystoscope, and the vessel fulgurated.

The newer meatome, which is now largely used, incises the ureter by endothermy current and no bleeding results, but the extent of the incision is more difficult to control and the wire not always easy of manipulation.

My own practice now is to have both instruments with me, but to use the scissors, stopping bleeding at the time of operation with a touch of a diathermy electrode and occasionally using the meatome as well.

With regard to actual manipulative removal of the stone, I have mentioned the use of multiple catheters passed beyond the stone, left in situ, twisted individually and then together and then withdrawn, and before mentioning other methods I should like to quote Bumpus: "It cannot, however, be too strongly emphasized that whatever the type of instrument that is passed up the ureter to engage the stone, it must be capable of removal from the ureter with the stone engaged, no matter in what position the stone happens to lodge in the instrument."

The Wellard-Howard spiral extractor, or corkscrew, is useful, and has had many successes, and has the advantage that if failure occurs it can be withdrawn by reverse action.

The Councill stone extractor forms a sort of wire cage and does not appeal to me, as it may nip the edge of a stone and be incapable of withdrawal; nor does the probang seem of much use. Caulk actually quotes one case in which he crushed a stone in the ureter with forceps!

Actual removal of the stone is a comparatively rare event, fortunately for the patient, who is thus relieved of further colic.

As adjuncts to these main principles, it is customary to employ medical measures. Plenty of fluids are important and the diuresis may prevent the increase in size of the stone. Belladonna is only of doubtful value, and while morphia must be given during really severe pain, it should be given sparingly so that Nature may not be unduly impeded in her good work, as colic (opposed to renal retention) is valuable. The injection of lubricants, liquid paraffin, olive oil, etc., round the stone, may be carried out simultaneously with the instrumentation and may be of help—and this is a condition where every little helps.

With regard to the immediate prognosis after manipulative measures, it is difficult to give rigid rules, some stones actually being observed to drop into the bladder during cystoscopy, probably just as a result of the anæsthetic, other cases taking six weeks to reach the bladder. This is apart from cases of failure.

With a moderate-sized stone held up at the ischial spine, about 4 cm. up the ureter, it is, however, often that the stone is voided into the bladder about the 17th day, so that in this type the patient should be led to expect this between the 14th and 21st days.

Mr. H. P. Winsbury-White: I have treated 76 cases of stone in the ureter. We are all agreed that a large percentage of ureteric stones will be passed spontaneously without instrumental interference. Two facts, however, are constantly present to the urologist, urging him not to wait indefinitely. One is the progressive damage which is being inflicted on the kidney; the other is that in spite of waiting, a certain number of stones will be permanently arrested. In these circumstances the proportion of cases which are assisted by instrumentation must of necessity vary according to the judgment of individual surgeons. In my own series there were 26% in which the stones were passed without any intervention. This group mostly consisted of those cases in which colic began for the first time just before they were seen. A most important group to recognize, because if X-rays reveal a stone of such a size as to afford a reasonable prospect of passing, the patient may be spared instrumental interference. Intravenous urography has shown that interference with renal function in these cases is temporary and is rapidly restored after the stone has passed.

The second group of cases consisted of those in which some instrumental assistance was required for the passage of the stone. 43% were treated in this way, of which 72% were successful. This group was made up of a few cases from the first group, in which, after the lapse of three or four weeks, the stone had failed to pass. There were others in which there had been no colic for many months and the stone was of such size as to be unlikely to pass unaided. The measures followed consisted of passing one or more ureteric catheters beyond the stone if possible, and/or slitting the ureteric orifice with the scissors or high-frequency electrode if the calculus lay on the pelvic floor. It was sometimes as long as one month after the orifice was slit before the stone was passed.

With regard to the passing of catheters: I would pass as many as possible, sometimes three, and leave them in position for six hours. 2% novocain and liquid paraffin were injected in a certain number of cases.

28% of my cases—22 in all—required open operation to remove the stone: 2 nephrectomy; 6 nephro-ureterectomy; 14 uretero-lithotomy.

In several of the nephro-ureterectomy cases, there were also stones in the corresponding kidney. Of the 22 cases requiring open operation, the stones were about equally distributed between the upper half and the lower half of the ureter.

There has been no mortality amongst the cases which I have treated, by any method.

Mr. E. W. Riches said he wondered why Mr. Wade preferred the iliac incision for stones impacted in the intramural part of the ureter ; a mid-line incision gave as good exposure of the lower ureter, and the bladder could be opened through the same incision if this became necessary.

He considered that incision of the ureteric orifice with the diathermy meatotome was the most useful transvesical manipulation for stones in the lower ureter. He mistrusted multiple-catheter methods as there was a danger of pushing the stone back.

With regard to medical measures, he had given glycerine by mouth in a small number of cases with varying success.

Mr. Alex. E. Roche : Some authors state that in 75% of cases they enable their patients to pass ureteric calculi by cystoscopic manipulations. We are also told (as we have heard to-night from Mr. Wade, and I believe it is true) that ureteric calculi are passed naturally, without such manipulations, in about 75% of cases. The similarity of these figures is suggestive that these manipulations are often needlessly and meddlesomely employed in cases of calculi which would pass naturally and unaided. I suggest that about 70% of ureteric calculi pass naturally, that from 10% to 20% require uretero-lithotomy or other open operation, and that the remainder are suitable for cystoscopic manipulations.

We are all liable to imagine that the passage of a stone after certain manipulations is necessarily due to these manipulations, whereas it might have occurred without them. I recently had under my care a young man with a ureteric stone which was within about an inch of the bladder, and which I felt convinced would pass naturally. However, as it was in exactly the same position after three months, I admitted him to a ward on a Saturday, intending on the Monday to cut the ureteric orifice with scissors passed through a cystoscope, but he passed the stone on the Sunday. Had I cut the ureteric orifice on the Saturday, I would have been tempted to think that the passage of the stone was due to the meatotomy.

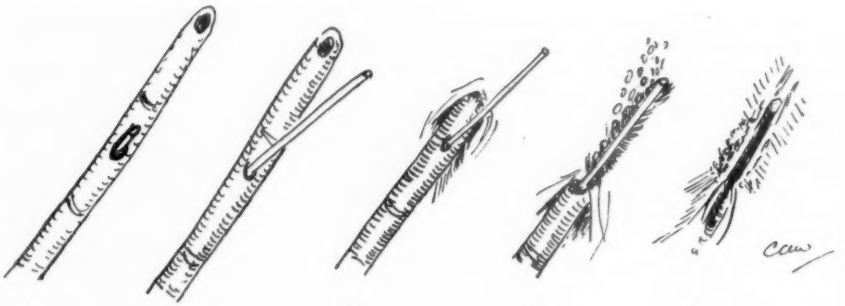
Expanding dilators and other such contrivances should be used only in the lowest inch of the ureter. It is safer to rupture the ureter into the bladder than higher up.

Mr. C. A. Wells said that a skiagram showing a stone with an extremely rough crystalline surface constituted a deterrent when accessing the suitability of a case for instrumental methods. Such stones adhered firmly to the ureteric wall and were not easily moved.

Referring to the statement that the use of scissors often caused troublesome bleeding when slitting up the ureteric orifice, this could be avoided by previous electro-coagulation of the area, a more rational procedure than coagulation after the bleeding had occurred. There was a simple method of opening up the orifice by means of the diathermy cutting current without the use of a special instrument (see fig. p. 30.) An ordinary ureteric catheter was prepared, with a fine stilette introduced so as to present at the lateral eye. When the catheter was in the bladder the stilette was pushed onward a quarter of an inch or half an inch. The tip of the catheter was then introduced into the orifice, the upper lip of which was thus engaged between the stilette and the catheter. The other end of the stilette was then connected

with the diathermy machine and the cutting current was turned on. A neat clean cut was obtained in this way and, if desired, it might be extended, without bleeding, by means of the scissors.

He wished to emphasize the value of injecting oil through dilating olives. Not only did the oil serve as a lubricant for the stone but it would frequently be found



Diathermy incision of ureteric orifice without special apparatus.
A.—Stilette at lateral eye. B.—Stilette advanced. C.—Catheter introduced. D.—Making the cut. E.—The cut ureteric orifice.

that the olive could be passed onwards in cases in which it was otherwise impossible to dilate the lower end of the ureter. The olivary bougies referred to were those of Professor Joseph.

[Mr. Wells showed lantern slides of a case in which uroselectan had been given three years after operation for ureteric stone. These demonstrated a remarkable degree of recovery from hydronephrotic dilatation affecting, not only the pelvis, but also the calyces, which had been dilated to three or four times their normal diameter.]

Section of Tropical Diseases and Parasitology

President—P. H. MANSON-BAHR, D.S.O., M.D.

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Plague: Modern Preventive Measures in Ships and Ports.

By C. F. WHITE, M.B.

ABSTRACT.—Maritime quarantine, introduced in the fourteenth century in an endeavour to prevent the spread of plague. Though the system failed to achieve its object, and was expensive and restrictive to sea-borne commerce, it survived for over 500 years, presumably because, in the absence of knowledge of the ætiology of plague, no method of procedure more likely to be successful could be devised. This country acknowledged the failure of quarantine as a preventive measure in the middle of last century, and substituted the medical inspection of ships on arrival, though the last Quarantine Act was not repealed till 1896. Nevertheless it was not till the discovery of the rôle of the rat and the rat-flea in the spread of plague that it was possible to establish plague-preventive measures on a sound scientific basis.

It is now recognized that a Port Health Authority must not only take steps to detect plague, human or rodent, afloat or ashore, at the earliest possible moment, but must eliminate conditions in ships and in shore premises which are conducive to the development of an epizoötic. Though here, and in other countries with an enlightened Public Health Administration, practice has long been ahead of legislation, the International Sanitary Convention of 1926 has now established throughout the world a large measure of uniformity in measures designed to prevent the spread of the more dangerous epidemic diseases by overseas trade, and the Port Sanitary Regulations 1933 have brought quarantine legislation in this country up to date.

For the detection of plague every ship arriving from a plague-infected port is medically inspected on arrival, but even if there is no evidence of plague-infection on board, such ships are examined daily by a rat-officer until the discharge of cargo is complete. Dead rats found and live rats trapped are bacteriologically examined. If a rat is reported to be infected the vessel is fumigated at once. The discharge of cargo is then continued under supervision, and when the ship is empty she is fumigated again. Shore premises, particularly those in the immediate vicinity of the berths of ships from plague-infected ports, are systematically searched for dead rats, and live rats are trapped. If evidence of plague-infection is found, energetic measures of rat destruction are at once instituted over a wide area.

The International Sanitary Convention requires all foreign-going ships to be inspected every six months as to the number of rats on board. If a ship is not so maintained as to keep the rat population down to a minimum she must be deratized.

If, after deratization, ships are to remain free from rats, they must be rat-proofed. Similarly ashore, rat-proofing is the only rat-repressive measure of permanent value.

The measures usually adopted to prevent the passage of rats between ships and shore are of limited value.

Finally, a rat-flea survey is of value in estimating the susceptibility of a port to infection.

RÉSUMÉ.—La quarantaine maritime fut introduite au 14e siècle pour essayer d'empêcher la propagation de la peste. Quoique ce système n'ait pas atteint son but, qu'il soit coûteux et qu'il ait un effet restrictif sur le commerce maritime, il persista pendant plus de cinq siècles, probablement parce qu'avant la connaissance de l'étiologie de la peste aucune méthode offrant plus de chance de succès ne pouvait être trouvée.

Dans ce pays l'insuccès de la quarantaine fut admis au milieu du 19e siècle, et l'examen médical des navires à leur arrivée fut substitué, quoique la dernière loi de quarantaine ne fut révoquée qu'en 1896. Toutefois ce n'est qu'après la découverte de la transmission de la peste par les puces de rat que la prophylaxie de la peste put être mise sur une fondation scientifique.

On reconnaît aujourd'hui que l'administration sanitaire d'un port doit non seulement découvrir la peste chez l'homme ou chez les rats, à terre ou à bord, aussitôt que possible,

mais doit éliminer les conditions dans les navires et dans les bâtiments à terre qui pourraient favoriser le développement d'une épizootie. Dans ce pays, et dans d'autres où il existe un service d'hygiène publique avancé, la pratique a depuis longtemps devancé la législation, et la Convention Sanitaire Internationale de 1926 a établi une grande mesure d'uniformité dans l'empêchement de la propagation des maladies les plus dangereuses par le commerce maritime, et les règlements sanitaires des ports de 1933 ont modernisé les lois de quarantaine dans ce pays.

Chaque navire arrivant d'un endroit où la peste existe est inspecté à son arrivée, mais même s'il n'y a pas de signe de peste à bord ces navires sont inspectés tous les jours par des chercheurs de rats jusqu'à la complétion du déchargement. Les rats morts et les rats vivants pris au piège sont soumis à un examen bactériologique. Si on trouve un rat infecté le navire est fumigé immédiatement. Le déchargement est continué sous inspection, et quand il est achevé le navire est de nouveau fumigé. Les bâtiments à terre, et surtout ceux dans le voisinage des ports d'amarrage des navires venant de ports où la peste existe, sont visités systématiquement à la recherche de rats morts, et les rats vivants sont attrapés. S'il y a des signes de peste des mesures énergiques pour la destruction des rats sont instituées dans une région étendue.

La Convention Sanitaire Internationale exige que tous les navires voyageant à l'étranger soient inspectés tous les six mois au point de vue du nombre de rats à bord. Si le nombre de rats n'est pas maintenu au minimum le navire doit être dératisé.

Pour maintenir les navires sans rats il faut qu'ils soient "rat-proofed." (Projections montrant les conditions favorables aux rats, et les manières d'y remédier.) A terre le "rat-proofing" est aussi le seul moyen permanent de supprimer ces animaux. (Projections illustrant de bonnes et de mauvaises conditions.)

Les mesures adoptées généralement pour empêcher le passage des rats entre les navires et la terre ont une valeur limitée.

Enfin, l'étude de l'infestation des rats par les puces est utile pour déterminer la susceptibilité d'un port à l'infection par le peste.

ZUSAMMENFASSUNG.—Die maritime Quarantäne wurde im 14. Jahrhundert eingeführt um die Ausbreitung der Pest zu verhindern. Diese Methode hat ihren Zweck nicht erzielt und war köstlich und für den Seehandel einschränkend, doch blieb sie für mehr als 500 Jahre bestehen, wahrscheinlich weil, wegen der Unkenntnis der Ätiologie der Pest keine besseren Massnahmen erfunden werden konnten.

In diesem Lande erkannte man das Versagen der Quarantäne in der Verhütung der Pest in der Mitte des letzten Jahrhunderts, und setzte die medizinische Inspektion der Schiffe an ihrer Stelle, aber das letzte Quarantäne Gesetz wurde nur in 1896 widerrufen. Es konnten jedoch pestverhindernde Massnahmen nur dann wissenschaftlich begründet werden, wenn die Rolle der Ratten in der Übertragung der Krankheit bekannt wurde.

Es ist heute erkannt dass es die Aufgabe der Sanitäts-Regierung des Hafens ist, nicht nur die Pest an Bord oder am Lande, bei Ratten oder bei Menschen so früh wie möglich zu entdecken, sondern auch die Zustände, die den Ausbruch einer Epizootie begünstigen, zu beseitigen. In diesem Lande, und in anderen die eine belehrte Gesundheits-Regierung besitzen, ist die Praxis schon lang im voraus vor der Gesetzgebung, aber die Internationale Sanitäts Konvention in 1926 hat eine weitgehende Uniformität in den prophylaktischen Massnahmen gegen die gefährlicheren durch den Seehandel verbreiteten Infektionskrankheiten festgesetzt, und die Sanitäts-Vorschriften für Häfen von 1933, haben die Quarantäne-Gesetzgebung in diesem Lande modernisiert.

Um die Pest aufzudecken wird jedes Schiff an seinem Ankommen aus einem pestinfiziertem Ort medizinisch untersucht, und auch wenn kein Zeichen von Pest vorhanden ist wird es täglich von einem Beamten auf Ratten untersucht bis die Ausladung beendet ist. Die gefundene toten Ratten und die gefangene lebendigen werden bakteriologisch untersucht. Wenn eine Ratte infiziert ist wird das Schiff sofort ausgeräuchert. Die Ausladung wird dann unter Beaufsichtigung fortgesetzt, und wenn das Schiff leer ist wird es nochmals ausgeräuchert. Gebäude am Ufer, besonders die in der Nähe von den Ankergrunden werden systematisch auf tote Ratten untersucht, und lebendige Ratten werden gefangen. Wenn Zeichen von Pest gefunden sind, werden energische Massnahmen zur Vernichtung der Ratten in einem grossen Bezirk unternommen.

Die Internationale Sanitäts-Konvention verlangt die halbjährliche Untersuchung aller ins Ausland reisenden Schiffen auf Ratten. Ist ein Schiff nicht in einem Zustand gehalten

der nur eine minimale Zahl Ratten erlaubt, so müssen die Ratten vernichtet werden. (Methoden zur Ausräucherung werden illustriert.)

Wenn man diese Schiffe rattenfrei halten will muss man sie gegen Ratten schützen. (Verhältnisse die der Ratteninfestation günstig sind und Methoden zu ihrer Verhütung werden illustriert.) Auch am Ufer ist die Schützung gegen Ratten die einzige dauerhafte Methode der Unterdrückung von diesen Tieren. (Günstige und ungünstige Verhältnisse werden illustriert.)

Die üblichen Methoden zur Verhütung des Übergangs von Ratten zwischen Schiff und Land sind wenig befriedigend.

Endlich ist eine Untersuchung auf Rattenflöhe sehr wertvoll in der Feststellung der Infektionsbereitschaft eines Hafens.

History of Maritime Quarantine

Communicable diseases have always travelled along trade routes. So long as international trade was on a small scale the spread of infection from country to country was correspondingly infrequent in occurrence and limited in extent. Though efforts were made at least as early as the sixth century to prevent the introduction of plague across land frontiers, it was not until the Middle Ages that any serious attempt was made to control the spread of disease by sea-borne commerce. In the middle of the fourteenth century the Black Death came to Europe and spread throughout the Continent, killing at least a quarter of the population and in some countries, including England, at least one-third.

Venice was then the great centre of trade with the East, whence came the plague, and in 1348 she appointed Overseers of the Public Health who were authorized to spend public money in isolating on an island in the lagoon any ships, persons, and goods suspected of carrying the infection of plague. In 1403 Venice established the first maritime quarantine station and in 1448 the Venetian authorities framed a code of Quarantine Regulations which served as a model for all others up to recent times. These prescribed that all merchants and persons coming from the Levant should remain in the House of St. Lazarus for a period of forty days and that cargoes of ships should be opened and aired for a similar period. Hence arose the terms "lazarette" and "quarantine." Genoa built a lazarette in 1467 and Marseilles one in 1476.

So far as England is concerned, though the merchants trading with Turkey adopted certain protective measures against plague and in 1664 the King in Council made regulations prescribing quarantine for vessels from the Levant, no Act of Parliament definitely establishing the practice of quarantine was passed until 1710, when there was alarm lest plague should be imported from the Baltic. Thereafter a number of Quarantine Acts were passed and a few examples of the burdens imposed on shipping may be of interest.

An Act of 1721 empowered His Majesty King George I to prohibit commerce for a space of twelve months with any country infected with plague. This Act continued in force for three years only, but the same powers were given again in 1727, together with power to prevent anyone coming from an infected place under penalty of £500. In 1731 two vessels laden with cotton-goods from Cyprus were ordered to be burned, with their cargoes. By the Levant Trade Act of 1752, vessels for the United Kingdom with foul "Bills of Health" were required to go to one of the lazarettes in the Mediterranean to have their cargoes sufficiently opened and aired. In 1780 vessels with grain from the Baltic had to lie forty days in quarantine and open and air the sacks. In 1800 two ships with hides from Morocco were ordered to be sunk off the Nore with their cargoes. The quarantine dues which had to be paid by shipping were enormous and it is not surprising that in 1824 a Select Committee on Foreign Trade drew attention to the serious financial burdens imposed on commerce by the existing quarantine methods. In the next year, 1825,

the last Quarantine Act was passed and remained in force until repealed by the Public Health Act 1896. It considerably modified the previous Acts but it still prescribed a period of quarantine for vessels coming from any place whence plague or other infectious disease might be brought; certain classes of goods had to be opened and aired, and persons on board were detained.

Though the Act of 1825 remained on the statute-book till 1896, the year 1831 was the last time a thorough maritime quarantine was attempted in this country. During the first half of the last century it was not plague, but cholera, against which quarantine was principally directed. It failed with the latter disease, as with the former, and after the experience of the cholera epidemic in 1831, the system was discredited and discarded in England.

It does not appear that when the next visitation of cholera came, in 1847, this country suffered more severely than other European countries which still rigorously enforced quarantine, and enlightened opinion of the time was admirably expressed by Sir John Simon who, as Medical Officer of the Privy Council in 1865, wrote as follows:—

"A quarantine which is ineffective is a mere irrational derangement of commerce, and a quarantine of the kind which ensures success is more easily imagined than realized. Only in proportion as a community lives apart from the great highways and emporia of commerce or is ready and able to treat its commerce as a subordinate political interest, only in such proportion can quarantine be made effectual for protecting it. In proportion as these circumstances are reversed it becomes impossible to reduce to practice the paper plausibilities of quarantine. The conditions which have to be fulfilled are conditions of national seclusion, and fulfilment of such conditions by England would involve fundamental changes in the established habits of the country." . . . "Now setting aside as not essential to quarantine the cruelties which its maladministration involves and which in practice are almost identical with its exercise; criticizing only the conditions which quarantine, if it is to be effective, must involve; and for the moment not even counting as an objection the cost of the gigantic establishment which has to be permanently maintained in order to meet occasional exigencies, I here insist only on the restrictions. Considering what they, when carried into effect, must involve—what inconvenience to persons, what interruptions to commerce, and on how vast a scale and for what indefinite duration—no one can expect that Governments, if they go so far as to enact, will have much success in enforcing quarantine. Against the efficiency of it when enacted there operate some of the strongest lawbreaking influences—on the one hand instincts of contempt for the narrow self-protectiveness which it represents and on the other those eager commercial instincts which now mainly govern the world. Contraband of quarantine, like ordinary smuggling, is developed as soon as the inducements for it are considerable. And thus, practically speaking, where great commercial countries are concerned, it can scarcely be dreamt that quarantine restrictions will be anything better than elaborate illustrations of leakiness."

Before this time efforts had been made to call together international conferences on the problems of quarantine, by France in 1838 and by England in 1843. In 1851 an international conference met in Paris, but England found that she could not accept its conclusions. In 1866 another conference in Constantinople made some progress, and conditions of quarantine were considerably modified. Further International Conferences were held in Vienna in 1874, in Washington in 1881, and in Rome in 1885. Gradually the weakness of the quarantine system came to be generally acknowledged, but it was actually not until the Conference in Venice in 1892 that the principle of dealing with ships according to the health conditions on board, instead of taking into consideration only the health of the port of departure, was widely accepted and that the first International Sanitary Convention was drawn up. True, this Convention dealt only with measures applicable to the Suez Canal to prevent the march of cholera towards the Mediterranean, but it was a beginning, and thereafter more rapid progress was made. The next year, 1893, a Conference in Dresden drew up a Convention for "the prevention of the propagation

and importation of cholera into healthy places." In 1894 the Conference in Paris regulated the Mohammedan Pilgrimage. In 1896 the reappearance of plague in Bombay and its rapid spread to other parts of the world created alarm and a Conference in Venice laid down the principles of international protection against this disease. Following the appearance of plague in Egypt in 1899, and the acquisition of new knowledge regarding the propagation of plague, an International Conference was again held in Paris in 1903, and for the first time an International Sanitary Convention dealing with both cholera and plague was formulated, and the establishment of a permanent International Health Office was proposed. In 1907, at the Rome Conference, the Office International d'Hygiène Publique was formed. This International Health Office, with its headquarters in Paris, has continued ever since to collect and distribute epidemiological information, and to discuss and issue reports and recommendations on matters of international public health interest, and has drawn up the International Sanitary Conventions of 1912 and 1926, dealing with maritime traffic, and, quite recently, the International Sanitary Convention for Aerial Navigation.

Meanwhile this country had pursued a more or less independent course. Having discarded quarantine in the middle of last century, England substituted the medical inspection of ships on arrival and dealt with them according to the health conditions on board. At first the Quarantine Medical Officers were attached to the Customs but in 1873 Port Sanitary Authorities were formed. The Public Health Act 1875 empowered the Local Government Board to make regulations for the prevention of the spread of cholera and other epidemic diseases on land or sea and the Public Health Acts 1896 and 1904 extended these powers. In 1907 the Local Government Board issued the Cholera, Plague and Yellow Fever Regulations. The Great War prevented these regulations from being amended to bring them into line with the International Sanitary Convention of 1912 but last year they were replaced by the Port Sanitary Regulations 1933, which follow closely the International Sanitary Convention of 1926.

It may seem that Europe generally was unduly reluctant to depart from quarantine, but it must be remembered that there was no knowledge on which to base a rational system of protection. Theoretically it must have appeared that quarantine ought to be effective and that the fault lay in the methods of application rather than in the principles on which they were based. England discarded quarantine partly because it was ineffective and partly because it was ruinous to her overseas trade, but she had not at the time any really efficient substitute, for we know now that medical inspection alone of ships on arrival is no guarantee against the importation of plague. However, being relatively isolated from the endemic centres of plague and cholera, she could afford to take risks which countries nearer to the danger were not prepared to face

So far as plague is concerned, it was not till the discovery of the rôle of the rat and the rat-flea in the spread of this disease that protective measures could be based on a sound scientific foundation and that every country could feel justified in surrendering the only weapon that had hitherto appeared to offer them any hope of keeping the enemy at bay.

Modern Methods of Plague Prevention.

These include arrangements for detection at the earliest possible moment of human or rodent plague in ships or on land, for the isolation of infected persons and the prompt destruction of infected rats and fleas, and for rat-repression both afloat and ashore.

I propose to give an account of procedure in the Port of London. The principles are those of the International Sanitary Convention, but the details of their application may not be suited in every respect to ports which are more susceptible to plague infection. The ideal of port sanitary administration is to provide the maximum

protection to the public health with the minimum of disturbance to trade. Procedure should therefore be nicely adjusted to the risks to which a particular port is exposed.

Detection of plague.—First then, as to the detection of human or rodent plague in ships at the time of arrival. The master of a foreign-going ship approaching a port in the United Kingdom must fill up and sign a Declaration of Health which is usually handed to him by the pilot. The Declaration of Health includes questions as to the occurrence on board of cases or suspected cases of plague and the existence or suspicion of rat plague or an unexplained rat mortality. If the reply to these questions is in the affirmative or if the ship has come from a plague-infected port she is boarded by a medical officer immediately on arrival. If the medical officer considers the ship to be an infected or suspected ship he orders her to the mooring station in the river, where she is dealt with as I shall presently describe. But even if the ship is passed as healthy she is not finished with if she has come from an infected port. She proceeds to her berth where she is visited by a sanitary inspector and an assistant rat-officer. Every available part of the ship is searched for evidence of rat-infestation and, particularly, for dead rats, and she is revisited daily so that holds can be searched as the cargo is discharged. Traps are also set to catch samples of the live rat population. Any rats found dead and also any trapped are sent for bacteriological examination for plague.

Ashore, the rat population is constantly kept under observation, particularly in the vicinity of the berths of ships from plague-infected ports, search being made for dead rats and live rats being trapped. Again, all dead rats and a proportion of the trapped rats are sent for bacteriological examination. I am aware that the existence of an epizootic, whether in ships or on shore, will usually be disclosed by the finding of dead rats and there are some who argue that it is therefore waste of time and money to examine trapped rats bacteriologically. But even in my limited experience I have known rats caught in traps to be plague-infected. I admit that in every case rats which had died of plague were also found, but it seems possible that, on occasion, an infected rat may be trapped before any dead rats are discovered, and since it is important to be aware of the existence of plague at the earliest possible moment, I have always considered it worth while to have trapped rats examined. Moreover, when a port has a regular and extensive trade with countries in which plague is endemic it is necessary in the interests of trade with uninfected countries to satisfy their health authorities that such port is really free from rat plague. It is not sufficient merely to state that there is no plague in the port ; evidence must be produced that the rat population in all parts of the port has been systematically sampled and found to be plague-free. Some ports rely for the diagnosis of rat-plague on naked-eye post-mortem appearances alone. In London a smear is made from the spleen in every case and examined microscopially.

If a rat is reported to be plague-infected it is obviously important to know exactly where it was found and therefore every rat sent for examination has a small label attached to one leg. On this label is a letter combination indicating the particular dock group in which the rat was caught or picked up and a serial number. The assistant rat-officer enters in his daily journal each letter-number combination with notes opposite showing where and how each rat was obtained. For transport to the bacteriological laboratory rats are placed in a linen bag saturated with paraffin, to ensure that fleas are killed, and are then enclosed in a tin box. Rats found dead, unless they are mummified or decomposed, or have obviously been killed, are taken for immediate examination. Trapped rats are delivered to the laboratory each evening at the end of the assistant rat-officer's day's work, and are examined next morning. In the case of a positive finding, the letters and figures on the leg-label are telephoned to the medical officer of health by the bacteriologist.

Fabian Hirst considers that plague has been carried from India to Ceylon by infected rat-fleas in the cargo of ships, without there being any rat-plague actually

on board. It would appear that this country is so far away from the endemic centres of plague that infected fleas could not survive in cargo from the time of loading abroad to the time of discharge here, and that therefore we need have no anxiety in regard to ships in which there is no evidence of a rat epizootic.

Control of plague infection.—The International Sanitary Convention defines a ship as "infected" by reason of plague if there is a case on board or a case developed more than six days after embarkation or if plague-infected rats have been found on board. A suspected ship is one in which a case of plague developed within six days of embarkation, or in which there has been an unusual and unexplained mortality amongst the rats on board.

Cases of plague are, of course, removed to hospital and the quarters occupied by the sick, together with their bedding and clothing, are disinfested. Close contacts are also disinfested if necessary. Passengers and crew are all medically inspected and their names and addresses are carefully checked and forwarded to the medical officers of health of the districts of destination where they are kept under surveillance for six days.

The human case of plague is, however, from the public health point of view, chiefly of interest as an indication of the probable existence of rat-plague on board. It is therefore necessary to prevent rats getting ashore and to destroy all rats and rat-fleas on board at the earliest possible moment. The ship must be isolated, either at moorings away from the shore or, if this is impracticable, at a specially appointed berth in the docks. If the latter course is adopted, the ship must be breasted-off from the shore at least six feet, the gangway must be well lighted and guarded, and lifted when not in regular use; all ports must be closed on the shore side and rat-guards must be placed on the mooring-ropes. I have long been of opinion that the guarding of mooring-ropes has received attention out of all proportion to its importance. I am aware that rats can easily run along a manila rope, and even struggle along a wire hawser, but I am satisfied that they seldom do so voluntarily. The exchange of rats between ships and shore usually takes place accidentally in cargo, particularly in bagged and crated goods. In some ports the decks of ships with low freeboard are practically flush with the quay, so that rats can just walk ashore, and may do so if food is scarce and their homes on board are disturbed, or if there is something particularly attractive in the adjacent cargo-sheds. Under such conditions it is obviously futile to put guards on the ropes without breasting the ship off from the quay. Again, it is often very difficult to guard all the ropes effectively and in many instances the type of guards used and their method of application are obviously farcical. For these reasons I am opposed to the customary general instruction that guards shall be fixed to the mooring-ropes of all ships. But, when a ship is infected, or suspected to be infected, with plague, every avenue by which rats might possibly reach the shore must be closed, and therefore in such cases guards should be placed on the mooring-ropes, but an effective type of guard should be insisted on, it should be placed on the right part of the rope and constant attention should be given to its position, which is liable to be disturbed by slackening or tightening of the ropes and by wind. From experiments, I believe that the best type of guard is a circular disc of sheet-metal with a raw edge and a smooth surface, three feet in diameter, maintained perpendicular to the rope and put on from the ship end as far from the ship's side as a man can reach.

Having moored the ship in an isolated position, the next step is to destroy the rats and rat-fleas on board by fumigation. It is not possible to guarantee a complete kill of rats in a loaded ship whether hydrogen cyanide, Clayton gas or the Nocht-Giemsa (carbon monoxide-carbon dioxide) method is employed. A moment's consideration will, I think, convince you that it is asking too much of any fumigant to expect it to reach every air-space in a cargo-laden hold in lethal concentration. Indeed Williams in New York, using hydrogen cyanide—the most diffusible and

deadly of fumigants—and carrying out the operation with the greatest care and skill only claims 80% efficiency. Nevertheless it is worth while fumigating a plague-infected ship at the earliest possible moment and then fumigating again as soon as the discharge of cargo is completed. But because it is not possible to insure a complete kill of rats in a loaded ship, the discharge of cargo should be carried out under supervision, bags and crates being examined before they are put overside and being opened up if it appears that they may be harbouring rats.

An alternative method is to discharge the cargo into lighters and fumigate each loaded lighter. This is a better method where it is practicable, because the cargo can be stowed in the lighter in such a way as to facilitate the penetration of the gas and, in the relatively small space, a lethal concentration can be ensured in every part; but it takes longer and is more expensive. Moreover, in many ports lighters are not available, and local conditions may make their use impossible.

The men engaged in discharging the cargo should wear overalls tied round the ankles and wrists and should be warned not to pick up any dead rats. Their names and addresses should be taken, and if any fail to turn up for work, inquiries should be made at their homes as to the cause of their absence. They should also be kept under surveillance for a week after they have finished working on the ship.

Ashore, in the vicinity of the berth of the ship, a careful daily search must be carried out for dead rats; rat-harbourage must be cleaned up and special efforts be made to trap, or otherwise destroy, any rats in the area.

When the ship is empty a final and very thorough fumigation should be carried out.

Such is the procedure when the ship is known to be an infected or suspected ship at the time of arrival. Unfortunately, it has much more often happened that on arrival there has been nothing to indicate that there is rodent plague in the ship —no human case and no knowledge of any rat mortality on board. The ship has proceeded to her berth, and at some stage of the discharge of cargo dead rats have been found. It is because this has so often been our experience that, so far as plague is concerned, I attach less importance to the routine medical inspection of ships from infected ports than to the careful inspection of the ship by a rat-officer every day until all the cargo has been unloaded.

The action taken under the circumstances is much the same as I have described for ships which are classed as infected or suspected on arrival. The discharge of cargo is stopped, the vessel moved to an isolated mooring station or at least breasted off from the quay and every precaution taken against rats gaining the shore or other ships. A preliminary fumigation is performed, the discharge of cargo is continued under supervision and, finally, the empty ship is fumigated from end to end. It is necessary in this event to pay special attention to investigating the possibility of infection having been conveyed to the shore rats, and if cargo likely to harbour infected rats has been already dispatched inland, it may be advisable to notify the medical officers of health of the districts concerned.

Though it is important not to lose time in dealing with an infected ship, it must be remembered that dead rats on a ship have not necessarily died of plague. It is not uncommon, particularly in grain ships, to find dead rats so decomposed or even mummified that bacteriological examination is of no value. I think sometimes they have died from lack of water and sometimes from asphyxiation. Naturally they cause us anxiety, but we are not stampeded into treating the ship as plague-suspected, though we are entitled to do so under the International Sanitary Convention and our own Port Sanitary Regulations 1933. We concentrate on efforts to obtain dead rats and live rats which can be bacteriologically examined. On the other hand, whenever the bacteriologist reports the finding of organisms resembling *B. pestis*, we always start plague preventive measures immediately without waiting for confirmation by culture and animal inoculation.

Prevention of plague infection.—It thus appears that, though knowledge of the

mode of spread of plague has enabled us to deal much more efficiently with infected and suspected ships, we may from time to time be taken by surprise and only discover the infection after the ship has been some days in the port and after infected rats have got ashore in cargo or otherwise. We come, therefore, to the most important plague preventive measures of all, viz., rat repression in ships and on shore, for it is obvious that if ships are practically rat-free an epizootic of plague is unlikely to occur, and, if it does, it will be limited in extent and will rapidly die out. Similarly if, on shore, the rat population is sparse, there is much less chance of any plague-infected rats which may land from ships giving rise to an epizootic.

The International Sanitary Convention take cognizance of both these points. The governments of signatory countries undertake to do all in their power to ensure that all requisite and practicable measures are taken by the competent authorities to secure the destruction of rats in ports and their surroundings as well as on lighters and coastal vessels.

In regard to ships, Article 28 of the Convention requires every foreign-going ship to be examined at intervals of six months as to the number of rats on board. If a ship is so maintained that any rat population is kept down to a minimum, she is granted a certificate of exemption from deratization which is valid for six months. If she is not so maintained then she must be deratized and is subsequently granted a deratization certificate which is likewise valid for six months.

The inspection of ships is carried out by rat-officers who, dressed in overalls and carrying electric torches, examine every part of the ship. The rat displays his presence by gnawing of woodwork, damage to cargo, runs, and feet and tail marks in dust, but chiefly by his droppings. In 1926, in Liverpool, I kept live rats in cages and counted the number of droppings each day. I was surprised to find that they passed on an average some fifty droppings, amounting to about a teaspoonful of excreta, every twenty-four hours. These experiments were further pursued by Pierce of Liverpool, who found that the number and size of droppings varied greatly according to the diet of the rats. On bran and wheat offal, the droppings were large and numbered as many as 120 per day. On rice the droppings were small—almost like mice excreta—and as few as 20 per day. Rat-officers must also be able to recognize the difference between fresh and stale droppings under various local conditions of temperature and humidity but with experience and careful observation they are able to make remarkably accurate estimates of the number of rats on board a ship.

If infestation is limited and localized and time is available, deratization may be achieved by trapping, but usually ships are deratized by fumigation. Formerly in this country sulphur dioxide gas generated by burning sulphur in open pans was always the method adopted. Now hydrogen cyanide is frequently used, having the advantages of being lethal in much lower concentrations, of being more diffusible and much quicker in action, and of not damaging cargo, coloured fabrics, paintwork, or metal. Its disadvantage is the risk to human life, in that a man may be killed before he is even aware of his danger. Originally, hydrogen cyanide was generated by mixing sodium cyanide and sulphuric acid, a process which required a lot of apparatus in which it was difficult to arrange to mix the reagents without exposing the fumigating staff to considerable risk, and in which the amount of cyanide generated was uncertain. To-day every method makes use of liquefied hydrocyanic acid gas. The liquid may be poured into containers and allowed to evaporate; it may be sprayed into the various compartments or it may be absorbed in some neutral absorbent which is scattered from containers on the floor of the various spaces to be fumigated. A lachrymatory warning gas may or may not be added to the cyanide but in any case it is never safe to conclude that, because the lachrymatory effect is not detected cyanide is not present in dangerous concentrations. With any of these methods three or four men can put a big ship under gas in a very short time and therefore the risk of fatalities is really very small.

In this country the Clayton system, in which sulphur is burned in a furnace and the gas propelled by fans into the ship and drawn back to the furnace and thus circulated round and round through generator and ship, has never been extensively used. In many ports abroad it is the only method employed and is stated to give very satisfactory results even in loaded ships. It is claimed that the dry gas does not damage cargo or fittings.

In the Nocht-Giemsa method a mixture of carbon monoxide and carbon dioxide generated from incandescent coke is driven into the ship. It is, I believe, still used in Hamburg where the Health Authorities have great faith in it.

There is no doubt that all these methods of fumigation are efficient if the concentration of gas and the period of exposure are carefully regulated and the ship is properly prepared for fumigation by the opening up of dead spaces so that the gas can enter freely. The Office International d'Hygiène Publique take the view that each authority should be free to employ any of the recognized methods and, while not laying down any standards the Office recommends the following:—

Hydrogen cyanide ...	2 ounces	per	1,000	cubic	feet	of space, with	2	hours' exposure
	or 1½ ounces	,,	,,	,,	,,		4	,, ,,
Sulphur, burned in open pots	3 lb.	,,	,,	,,	,,		6	,, ,,
Salforkose (a liquid mixture containing carbon bisulphide)	2 lb.	,,	,,	,,	,,		4	,, ,,
Vapourization of liquid sulphur dioxide ...	4 lb.	,,	,,	,,	,,		4	,, ,,

Clayton gas: Continue until the concentration of sulphur dioxide issuing from the upper part of the compartment reaches 2% by volume or burn in the generator 3 lb. of sulphur per 1,000 cubic feet of space treated and give two to three hours' exposure.

In rat-destruction ashore, fumigation, except of rat runs by sulphur or cyanogas, is seldom practicable and trapping and poisoning are usually employed.

I have dealt with methods of rat-destruction first, but the most important rat-repressive measure and the only one which will give results of permanent value either in ships or on shore is rat-proofing.

Rat-proofing means eliminating enclosed spaces in which rats may nest and breed, or at least making such spaces inaccessible to rats, and preventing the access of rats to supplies of food and water.

Potential nesting or breeding places are termed rat-harbourage. A house is still a house even if it is unoccupied and so rat-harbourage is still rat-harbourage even if at the time of inspection no rats are making use of it. It is usually easier, particularly in ships, to eliminate or protect rat-harbourage than to cut off supplies of food and water. Sometimes it is easier to prevent rats from obtaining water than to deny them access to food. The complete programme of rat-proofing comprises the prevention of nesting, feeding and drinking, but if it is not practicable to do all three, it is worth while depriving the rat of two, or even only one, of these necessities of life.

It is very difficult completely to annihilate a rat colony by trapping, poisoning or even fumigation. Usually there are a few survivors, and rats are so prolific that they quickly breed up to the limits of the nesting accommodation and the food-supply. But even if you are fortunate enough to destroy every rat in a building or a ship it is certain that good homes for rats will not long remain untenanted and the methods of deratization must be repeated again and again.

The majority of rats in ships are probably born on board and every ship has a certain maximum rat capacity. I am aware that from time to time we do get sudden invasions of ships by large numbers of rats, but this is the exception and not the rule. I know, too, that there is a certain interchange between rats ashore and those afloat. But at the same time I feel sure that rats do not voluntarily leave a comfortable home. Increase of population or scarcity of food-supply may enforce migration. I suppose

there are some rats which are naturally wanderers and perhaps romance or domestic difficulties may cause some others to leave home. I understand also that on the occurrence of a severe epizootic of rodent plague rats will flee from the infected area. But I think that rats which are well housed and well fed will settle down to a comfortable family life and have large litters at frequent intervals. Our best method of waging war on rats is therefore to present them with an acute housing-problem and a food-shortage. Then we may be sure that their birth-rate will go down and their infant mortality and general death-rates will go up.

In ships rat-proofing has an additional advantage in that it increases the efficiency of fumigation. There are, in many ships, spaces which are accessible to rats but to which no fumigating gas, not even hydrogen-cyanide, can penetrate in lethal concentration during any ordinary fumigation. So much has been said of the toxicity of hydrogen-cyanide and of the danger to human life in cyanide fumigations, that I find a tendency on the part of shipping people to believe that the gas will penetrate everywhere and kill everything. But in actual fact no fumigant will get through small openings into comparatively large dead spaces where there is no movement of air, for the physical process of diffusion is relatively slow and the distribution of a fumigating gas through a ship depends largely on internal air currents or draughts inside the ship, set up by differences of temperature and wind pressures. Such dead spaces are precisely those chosen by rats for nesting and hiding when they are disturbed, as they frequently are during the day-time, when a vessel is in port. For effective fumigation such spaces must be opened up to enable the gas to enter. It is obviously better to eliminate these harbourages, or to make it impossible for rats to get into them.

There is another important advantage in rat-proofing. Eskey's investigations in Peru and Ecuador have demonstrated that where rat-harbourage is abundant the rat-flea index and particularly the "cheopis index" is high. Indeed, without proper harbourage, rats have a "cheopis index" too low for the continued transmission of plague. Thus rat-proofing is a double insurance against bubonic plague, not only reducing the number of rats but also reducing the number of plague-carrying fleas, on such rats as may survive.

The broad principles of rat-proofing are quite simple. They are:—

(1) Eliminate all enclosed spaces which might be used by rats for hiding or nesting or, if it is impracticable to eliminate such spaces, protect them with galvanized sheet-metal or expanded metal of not more than half-inch mesh, so that rats cannot get into them.

(2) Close all openings through which rats might pass from one compartment to another in search of food or water or to escape from fumigating gases.

Rats seldom gnaw on flat surfaces but nearly always at edges, corners or angles, and therefore it is these points that need attention in protective work.

The details of the application of the principles of rat-proofing to ships are elaborate and technical, but I think that anyone who fully understands the principles, and is trained in observation, could go into a compartment of a ship and suggest where rat-proofing was necessary. I must acknowledge my indebtedness to Mr. Holsendorf, Officer-in-Charge of the Rat-Proofing Division of the New York Quarantine Station who has spent years in the study of the rat-proofing of ships and has worked out all the practical details in co-operation with naval architects and ship builders.

There is no doubt whatever that the rat population in ships has been greatly reduced in recent years. This is due partly to the operation of Article 28 of the International Sanitary Convention of 1926 to which I have already referred, partly to the fact that the natural tendency has been to build ships which provide less rat-harbourage and partly to the fact that appreciation of the value of rat-proofing is gradually spreading amongst those who build, own and operate ships.

The same principles of rat-proofing apply ashore, but the problem is often more difficult than in ships. It is quite easy to see what requires doing, but it is not so easy to get it done. I would, however, like to urge that even if a complete programme cannot be carried out, every little bit of rat-proofing that can be done is worth while. It may be that structural alterations are not possible, but in the last resort even ordinary cleanliness in premises and tidiness in the storage of goods and gear of various sorts will have beneficial effects.

Finally, I would suggest that it is always worth while estimating the susceptibility of a port to plague infection. I understand that *Xenopsylla cheopis* is the most efficient plague-transmitting flea, and that therefore the ease with which plague may be spread amongst the rat population of a port may be more or less gauged by estimating the average number of cheopis fleas per rat. The figure thus obtained is called the "cheopis index." If the "cheopis index" is less than 1, rat-plague will not easily spread; as the index rises above 1 so does the danger of infection increase.

During 1932-33 we carried out a "flea-count" on the rats in the Port of London. The method of procedure was prescribed by Professor Buxton of the London School of Hygiene and only rats caught singly and alive were examined. This requirement restricted very considerably the number of rats available for the investigation, because many rats are caught in killing traps and when cages are set it often happens that more than one rat is found in a cage. The actual combing of rats and the diagnosis of the fleas were carried out by Dr. E. Kean.

In all, 1,094 rats were examined, 683 black and 411 brown. On only two rats, one black and one brown, were *Xenopsylla cheopis* found. Both were caught during September 1933 in the South West India Dock, adjacent to the berths of ships from India and the Persian Gulf. The average number of fleas per rat was 3. The predominant flea was *Ceratophyllus fasciatus*, the average number per rat being 2·5. Other fleas found were *Leptopsylla musculi*, *Ctenophthalmus agyrtes*, and *Ctenocephalus felis*.

Although the investigation was primarily concerned with shore rats, 88 black rats and 2 brown caught in cages in ships or picked up after a ship had been fumigated with hydrogen cyanide, were examined. No less than 80 of these rats were found to be entirely free from fleas, but 10 yielded 52 fleas, of which 21 were *Xenopsylla cheopis* and 31 were *Ceratophyllus fasciatus*. The cheopis fleas were all obtained from four rats, caught singly in traps in ships from Vancouver, Cuba, and Braila.

These observations serve to confirm our belief that at the present time ports in the United Kingdom are not susceptible to infection with rat-plague.

But immediately after the Great War, plague-infected ships were not so uncommon as they are to-day, and limited outbreaks of rat-plague did occur in English ports. Though I do not believe that there was even then any real danger of an epidemic of plague in this country, I have reason to remember the effect on shipping of any suspicion abroad that rat-plague existed in one of our ports, and I therefore feel that we must continue to take the precautions I have described, if not as a public health measure, at least as a trade-protective measure. Moreover, the prevention of the spread of plague is an International problem. By the ratification of the International Sanitary Convention certain obligations are undertaken; surely these obligations should be fully discharged in the principal port of what is still the principal maritime nation of the world.

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Section of the History of Medicine

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The History of the 1832 Cholera Epidemic in Yorkshire

By E. ASHWORTH UNDERWOOD, M.B., D.P.H.

THE history of Asiatic cholera in this country is interesting, not only because the disease was entirely unknown to British practitioners before the "thirties" of last century, but also because of the light which the first outbreak threw on the glaring social and sanitary abuses which existed a hundred years ago. It is true that the profession had been warned that the disease was epidemic in the East, but only those practitioners who had had Indian experience could form any conception of the possible ravages of cholera. On the social side, the epidemic in Britain was directly responsible for the reporting of conditions which had hitherto been regarded as the unalterable lot of the poor—conditions which were regarded by most of the rich as belonging to a world with which their own contact was of the slightest.

Asiatic cholera became epidemic in the East in 1817, and the disease continued to reap a terrible toll of life for many years. It first appeared in this country at Sunderland in August 1831. The approaching outbreak was not unexpected; on June 21, 1831, a Board of Health was gazetted in London in anticipation of the event, and it was suggested that local Boards of Health should also be set up. An excellent account of the working of such a local Board was given by Shapter [1], and I have previously commented upon the administrative difficulties which beset the path of these boards [2].

In the annals of the 1832 cholera epidemic in this country attention is not usually focused on the ravages of the disease in Yorkshire. Yet in this county there were 1,960 deaths [3]. This neglect is not surprising, for some of the published descriptions of the individual outbreaks are very rare. Leeds especially has suffered from omission at the hands of the historian. Yet the township of Leeds was severely affected. The total deaths in Leeds were almost half of the deaths for the whole county, and this total was approximately equal to the deaths in Manchester and in Plymouth, and it was exceeded only by the deaths in London, Liverpool and Newcastle.

It is probable that the first death from cholera in Yorkshire occurred at Doncaster on January 7, 1832. Branston[1] [4] states that two sailors arrived at the town on the evening of January 6. They had been to Stockton, Hull, Leeds, and Wakefield. They stayed overnight at a lodging-house, and next morning one of them was seized with symptoms which were very suspicious of Asiatic cholera: he died within a few hours. No outbreak followed this incident. There is no doubt, however, that in Doncaster the occurrence caused considerable perturbation. I have previously commented [5] on a popular pamphlet which was published in that town, and dated January 21, 1832. The pamphlet is entitled "*Cholera morbus. Precautions, Preventives and Remedies, compiled by a Clergyman for the use of his Parishioners.*" In the main, the advice followed the official instructions which were issued from time to time by the Central Board of Health.

[1] In the literature of the period this name occurs both as "Branston" and "Branson," cf. references [4] and [9]. The person referred to was the Chairman of the Doncaster Medical Board of Health.

In Yorkshire generally various cases were reported during February and March; these were later shown not to be cases of true cholera. In the first week of April, however, the disease broke out at Goole, and almost simultaneously at Hull. On April 6 a man in Hull developed suspicious symptoms, but he recovered [6]. On April 13 a man died in a south-western suburb of Hull, and both these cases were marked "cholera" by the Central Board of Health, which considered the port infected as from April 6. It is probable, however, that the first authentic death from cholera occurred on April 13. It was later discovered that five days before, a man had been helped ashore from a steam-packet which had come from London, and this man died on April 15. Subsequent inquiries showed that he had been admitted to St. Olave's Cholera Hospital in London on March 29, suffering from a severe attack of the disease, and that he was discharged "convalescent" on April 6. It is tempting to assume that this man was the means whereby Asiatic cholera was introduced into the port of Hull. From Alderson's [6] description it would appear that the disease did not produce a great number of deaths until June, when it broke out again with renewed virulence in a poor north-western suburb.

From the descriptions in the literature it is evident that the disease became epidemic throughout Yorkshire about the end of May or the beginning of June 1832. The disease appeared at Leeds on May 28 [7]; at York on June 2 [8], and at Doncaster on the same day [9]; at Cawood, near Selby, on June 5 [10]. A death, which was probably due to cholera, was that of an immigrant into Sheffield on June 14. It is fairly certain, however, that the Sheffield epidemic did not commence until July 8. At Wakefield it affected the House of Correction on June 23, and in a mild type it persisted there for a long period [11]. While the epidemic lasted it caused the deaths of 1,960 persons in the county. The most important places which were affected were: Leeds, 702 deaths; Sheffield, 402; Hull, 300; York, 185; Wakefield, 62 deaths. Bradford, Goole, Selby, Rotherham, Whitby, and Doncaster had each fewer than 40 deaths. Where so many districts were affected, it is obviously impracticable to deal with all the foci of disease. In this paper, therefore, emphasis will be placed mainly on the outbreaks at Leeds, Hull, and York. These outbreaks were all fairly fully described, and, in addition, the reports from Leeds are especially valuable in throwing light on the sanitary conditions which obtained at the period. I have decided not to go into any detail with regard to the Sheffield outbreak, and in doing so I have been influenced mainly by the fact that Stokes [10A], in a book published in 1921, made a very valuable collection of the writings dealing with that outbreak. These writings were mainly official reports and extracts from the lay press. Although they do not add considerably to our knowledge of the medical or epidemiological aspects of cholera, they are very valuable in that they describe fully the administrative procedures carried out in these days.

The essential information concerning the Leeds outbreak is contained in a report by Dr. Robert Baker, a District Surgeon to the Leeds Board of Health [7]. The report is dated January 3, 1833.

The actual introduction of Asiatic cholera into Leeds was preceded by a general tendency to bowel complaints, and violent diarrhœa was not at all uncommon. This "diarrhœal tendency" was often referred to about this time. For example, John Parkin [12], writing in 1841, says:

> "This phenomenon was particularly observed during the prevalence of the epidemic cholera; for not only was the severe form of the malady preceded for many days by slight attacks of diarrhœa, but a variety of anomalous symptoms, indicative of derangement in the digestive organs, was observed to prevail for many weeks before the epidemic manifested itself in its most severe form. To this particular affection the term *cholerine* was applied by the French."

Shapter [1] also describes this milder form of disease under the term "cholerine," and he indicates that it was common in Exeter at the time of the cholera epidemic. Shapter says that it was characterized by

"tinglings of the surface, weakness and numbness of the limbs, slight spasms, feelings of languor and depression, often accompanied by a flatulent dyspepsia or diarrhœa, in which the discharges were occasionally of a light colour."

Shapter did not decide whether this condition was a mild form of true cholera, or whether it was an "accidental accompaniment of the period." He does note, however, that persons who had experienced these milder symptoms did not appear to be exempt from true cholera. No extended description is given by Baker of this condition in Leeds, but it probably resembled Shapter's "cholerine" very closely.

In 1832 the town of Leeds had a population of 76,000 persons, and it was surrounded by a number of small townships which have since been incorporated into the modern city. The first case of true cholera occurred in a child, aged 2 years, who lived in a small dirty cul-de-sac called the Blue Bell Fold. It would appear from the report that the date of this occurrence was either May 26 or 28, 1832—more probably the latter date. The child became ill in the morning and died at 5 p.m. on the same day. On the following day, May 29, a play-fellow, who lived a few doors away, was attacked and died in about twelve hours. Baker says that, although it was known that cholera was then present at Selby and Goole, no connexion could be traced between these towns and the first case. He is, however, evidently unwilling to admit contagion as a cause of the outbreak. Speaking of the direct contact which was proved between the first and second cases in Leeds, he says:—

"This would have looked something like contagion, had it not happened that in the course of the week three cases occurred in individuals at a considerable distance from the Blue Bell Fold, where there had been no connexion with the former families."

The greater part of the Report is an incrimination of unpaved streets and yards as causes of the disease. There is, however, a valuable appendix, in which particulars are given which enable us to trace the course of the disease in the community. Cases continued to occur in different parts of the town, and by the end of the first fortnight in June widely separated districts had been affected. A reference to the "cholera map" which is attached to the Report shows that the incidence was certainly highest in the north and north-east quarters of the town, that is, in those parts which are still densely populated. Those parts of the town which lay south of the River Aire were comparatively little affected. The distribution of the epidemic in time is given in the following table:—

	Cases	Deaths
May 28	2	1
June	164	42
July	427	167
August	668	273
September	334	123
October	216	73
November (up to 12) ...	6	3
Total	1,817	702

The epidemic reached its height on August 16, on which day there were 59 new cases and 21 deaths. With a water-borne epidemic of this type we would have expected multiple cases in households to be very common. In point of fact, this does not seem to have been the case, since Baker gives the following particulars: In 53 families two persons were attacked in the same house at the same time; in seven families, three persons; in three, four persons; in one, five; and in one, seven persons.

The age and sex distribution of the cases and deaths is given in an appendix under the curious title of " A Calculation on the Probabilities of Human Existence in Persons attacked by Cholera, in every age, from six months to ninety years, both inclusive." From this table the following abbreviated statement of the age and sex distribution of the 1,817 cases has been compiled :—

LEEDS CHOLERA (1832).

AGE	-5	-10	-20	-30	-40	-50	-60	-70	70+	AGE UNKNOWN	TOTAL
CASES	151	139	193	215	307	310	179	125	77	121	1817
DEATHS	76	45	51	60	89	104	100	80	56	41	702
CASE-MORTALITY PER CENT.	50	32	27	28	29	34	56	64	73	-	38.7

It is evident from the Report that considerable care was taken to make the returns as reasonably complete as could be expected at that time. There is, therefore, some justification for accepting the conclusion that the case mortality rate for the Leeds epidemic was somewhat higher than the rate (33%) which was generally experienced at that period. We see also that the disease was very fatal in the early years of life. During maturity the chances of recovery were more favourable, but the case mortality rate again increased rapidly and progressively after the age of 50 years.

It is interesting to compare the incidence of the disease in Leeds with its progress in York. The outbreak in the latter city was well described by Needham [8]. It has already been stated that cholera broke out in York on June 2, 1832. The epidemic was not unexpected, and, by order of the officials of the City, precautions were taken to prevent the spread of the disease from Goole, Hull, and Leeds. The poor were fed, and in very needy cases their rooms were whitewashed at the public expense. Needham says that the epidemic appeared just at the end of York races, and the disease

> " was beyond all doubt introduced by some of the ragged and beggarly 'gentlefolk' who had come to be present at our 'festivity,' and to profit as largely as they could by the folly and vices of other people."

Many of the earliest cases were in vagrants, who were known to have come from Selby, Hull, and Leeds.

The earlier history of the York outbreak presents an interesting exercise in epidemiological speculation. (i) Thomas Hughes, aged 21 years, who lived in a street near the River Ouse, had been employed on May 28 in ferrying across the water persons of all kinds from Selby, Hull, and Leeds. On June 2 he was stricken with cholera ; he recovered. (ii) On June 7, his brother William was attacked. (iii) On the 8th, John Hughes, the father of these two young men developed cholera. (iv) When Thomas Hughes was first taken ill he called at the house of his uncle, James Kendle, who resided on the opposite side of the river. On June 12, Kendle was attacked, and (v) on the following day his daughter was also affected. (vi) On June 5—i.e. three days after the definite onset of the disease in the first case—John Graves, who resided in the same court as the Hughes family, was affected. Needham notes that he used the privy into which the evacuations of the Hughes' patients were cast. (vii) On June 12, the wife of John Graves was affected. And so on. In the light of this evidence it is difficult to see how the question of some common factor could have been avoided. The disease now progressed fairly rapidly at York, but from the daily returns which Needham gives it would seem that many cases must

have escaped unnoticed. The peak of the epidemic appears to have been reached about July 1 and 2, on which two days 44 cases were recorded, and 17 deaths occurred. The disease did not finally disappear until the middle of October. During the whole outbreak 450 cases were considered to be cholera, and 185 deaths occurred. From a table which is given the following summary of the age and sex in 185 fatal cases has been compiled :—

YORK CHOLERA (1832)

AGE	-5	-10	-20	-30	-40	-50	-60	-70	70+	UNKNOWN	TOTAL
MALE	7	5	8	7	9	15	23	15	15	[12]	104
FEMALE	3	4	1	17	14	8	8	7	7		69
TOTAL	10	9	9	24	23	23	31	22	22	[12]	173

The outstanding feature of this table is the preponderance of male deaths over the age of 40 years. On the figures which Needham gives, the case mortality was 41%—and is thus considerably greater than the case mortality for Leeds. It has been mentioned, however, that in York many of the cases were probably not reported.

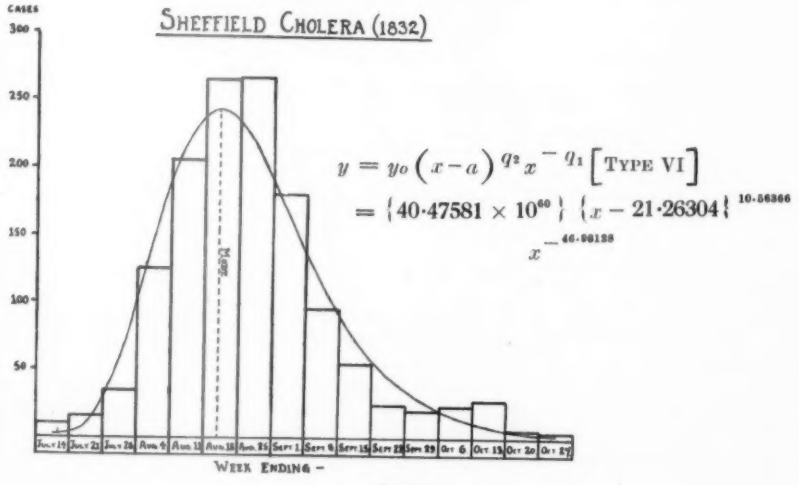


FIG. 1.

I was interested to see how far the available data for these epidemics could be treated on modern lines. It has been mentioned that the figures for the Sheffield epidemic, as given in the reprints of reports which are collected in Stokes' book [10a], are apparently complete. The cases, week by week, are shown in the form of a histogram in fig. 1. I found that it was possible to fit a Pearson's Type VI curve

to these data, and the actual frequencies week by week, with the corresponding theoretical frequencies, are given in the following table:—

Week ending:	Actual cases	Cases as calculated from the curve
July 14	10	0·2
„ 21	15	8·7
„ 28	36	57·3
August 4	124	145·8
„ 11	204	220·0
„ 18	266	241·6
„ 25	267	215·3
September 1	180	166·3
„ 8	94	117·0
„ 15	56	73·5
„ 22	24	46·3
„ 29	19	27·4
October 6	23	15·8
„ 13	28	8·9
„ 20	6	4·9
„ 27	3	2·7

The theoretical frequencies are plotted as a smooth curve in the figure, and it will be seen that the fit is fairly good, considering the age of the data.

It was more difficult to treat the Leeds data in a similar fashion, because detailed figures were not given for the first four weeks. By applying the frequency which occurred week by week during the first five weeks in Sheffield to the Leeds data, an approximate frequency was obtained for the start of the Leeds epidemic. When the total figures were dealt with in three-weekly periods it was found that a reasonably good curve was obtained. A Pearson's Type I curve was found to fit these data best, and the following table shows the actual and theoretical frequencies:—

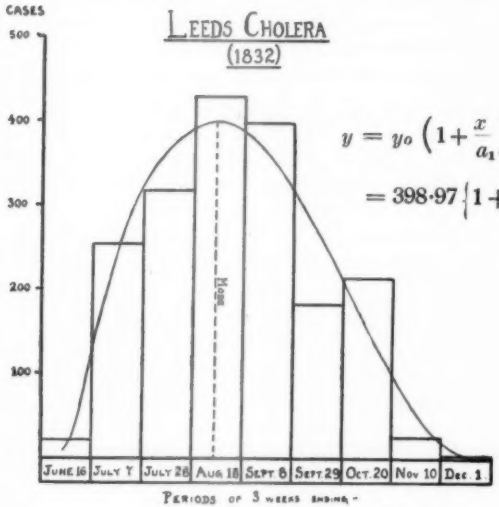
Period ending:	Actual cases	Cases as calculated from the curve
June 16	21	11·3
July 7	253	230·9
„ 28	318	361·2
August 18	428	398·9
September 8	399	359·5
„ 29	182	268·9
October 20	216	152·9
November 10	27	47·1
December 1	2	—

These results are set out in fig. 2. It will be seen that a good curve is again obtained.

The actual cases for the York outbreak are shown in the form of a histogram in fig. 3. The distribution was so irregular that no attempt was made to fit a suitable curve.

These data suggest that the figures which are given in the records for the epidemics at Leeds and at Sheffield are probably quite accurate, despite the fact that they were compiled over a hundred years ago. Further, when we compare the two theoretical curves, for Leeds and for Sheffield respectively, we see that the Sheffield epidemic differs in important respects from the Leeds epidemic. At Sheffield the rise to the peak—that is, the mode—was rapid, and was effected in less than five and a half weeks; but thereafter the disease continued to prevail, and it was a further ten weeks before the infection subsided. In Leeds, on the other hand, the epidemic took ten weeks and a half to reach its peak, and, comparatively speaking, the decline was somewhat more rapid; in actual fact the decline took about sixteen weeks. Generally we may say that the Sheffield curve was much more typical of cholera than was the Leeds curve.

The clinical features of Asiatic cholera in Leeds are not dealt with in Baker's Report. This is somewhat unfortunate, because in the year 1832—probably before the actual cholera outbreak—a short treatise on this disease was published in Leeds by Charles Turner Thackrah (1795-1833) [13]. This author was a pupil of Sir



$$y = y_0\left(1+\frac{x}{a_1}\right)^{m}\left(1-\frac{x}{a_2}\right)^{m_2}\ [\text{TYPE 1}]$$

$$= 398{\cdot}97\left\{1+\frac{x}{3{\cdot}00322}\right\}^{1{\cdot}093141}\left\{1-\frac{x}{4{\cdot}95059}\right\}^{1{\cdot}801963}$$

FIG. 2.

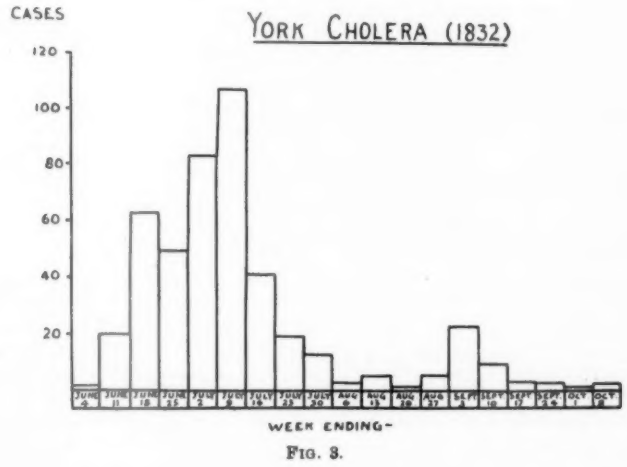


FIG. 3.

Astley Cooper, and in the same year he published one of the first treatises on industrial dust diseases. Thackrah discusses the main types of cholera, and it is evident that, in his description of the Asiatic type, he is drawing, not on his own experience, but on the descriptions of Indian surgeons. The main interest of his

work for us is that he gives an excellent description of an outbreak of "cholera" which affected Leeds and the surrounding townships in 1825. This outbreak is briefly referred to by Creighton. Thackrah made a house-to-house survey in certain districts for the purpose of ascertaining the extent of the infection, and he was accordingly in a position to describe the disease comprehensively. The outbreak commenced in May 1825, but cases were not numerous until August. The disease prevailed until December. The symptomatology was striking:

"purging and vomiting, cramp, coldness of the extremities, and prostration of strength."

The disease was frequently severe, and the stools often resembled "gruel or barley-water." The point of interest is that Thackrah argues that this type of cholera which he saw in 1825 was identical with the Asiatic cholera which visited the town seven years later. His argument is amusing. After giving a full description of some severe fatal cases which he saw, he continues:

"No two cases can in any country, or of any disease, be expected to have precisely the same symptoms. But I contend that the signs which are considered to characterize the Indian Cholera are found in a marked and decided degree in the cases just stated. Thus we have the peculiar character of the evacuations—the sudden and great prostration of strength—the extraordinary reduction of pulse—the shrunk and purple countenance—the loss of voice—the purple, or pale, contracted state of the extremities—and death sometimes in a few hours. I conceive, therefore, that no fair reasoner can refuse to admit the identity of the disease. A physician sent down by government to ascertain the character of the Cholera in the north of England has repeatedly declared that he could distinguish the Indian from the English *only* by the *prevalence* of the former—the *number*, not *nature*, of the cases giving the distinctive character of the Indian. Cholera in England has certainly not produced as great a mortality as Cholera in India. Neither has inflammation of the liver; yet no one considers Indian Hepatitis as distinct in nature from English."

In his treatise Thackrah mentions 339 cases of "cholera" which he had seen, or about which he had information. Only six of these were fatal. A comparison of these figures with the case mortality of nearly 39% which the true cholera showed when it did reach Leeds, does not lead us to doubt the historical assertion that Asiatic cholera was not seen in this country before 1831. There is little doubt that Thackrah's outbreak was one of "cholera nostras."

To return to the 1832 epidemic. We may infer the clinical findings in Leeds from other writings of the period. The best which I have encountered are those of Shapter [1] for Exeter. An epidemic which was geographically closer to Leeds was that at Hull, and Alderson's description may be used [6]. It has been stated that the outbreak started in Hull during the second week of April 1832, and there were 300 deaths before it subsided. Alderson lays most stress on the barley-water discharges as a characteristic symptom. He says:

"So great in some cases is this discharge, that it is not unusual to find the apartment completely inundated with watery fluid, which has passed from the bowels . . . through the bed of the patient."

He describes the vomiting as being of a peculiar type—

"sudden, without retching, and ejected in large quantities, as if pumped from the stomach."

At Hull the cramps do not appear to have been so marked as they were in some other localities. He speaks of

"the dark purple hue of the face and extremities, and corrugation of the skin of the hands and fingers."

In the state of true collapse he says

"the eyes have been much depressed, and the voice almost lost; what remains consists of a peculiar whisper, with, in some cases, a shrill syllable now and then involuntarily escaping."

Alderson gives a minute description of the different types of evacuation. In the consecutive fever of the Hull cases he says that hiccup was a prominent feature, and it apparently occurred most frequently in fatal cases.

Needham [8] says that at York diarrhœa was a very general premonitory symptom. In some cases it was of very short duration, but in many it lasted a week or more before the typical features presented themselves. The collapse stage at York never lasted more than forty-eight hours; before the end of this period the patient either died or showed symptoms of reaction. Delirium was quite frequent. Needham also states that the most rapid cases of collapse were those in which the stomach manifested the greatest irritability. The consecutive fever he had known to continue for eight days.

Contemporary reports of the pathology of the disease are not very interesting. Most of them emphasize the essential features. For example, Bell [14] gives a good description of the gorged appearance of the veins. He says that the internal coat of the stomach, and sometimes of the duodenum,

"has very generally a peculiar appearance; there are vascular patches, not of inflammation, but as if vessels had burst, and blood had been extravasated between the coats. These spots, though no doubt commonly a congeries of congested veins, do certainly sometimes arise from extravasation. Patches also are described as having the character of inflammation, generally near the pylorus; which are by some considered the result of local irritation, produced by portions of the remedies prescribed having adhered to these parts of the stomach; and they must be taken as a proof that reaction had commenced before death."

This description applies to cases which Bell saw in India. Alderson [6] at Hull described how

"the mucous glands were seen in groups much enlarged, and here and there occur patches of dark brown spots, indicating the presence of diseased mucous follicles, with the appearance of a deposit of the red particles of the blood beneath the membrane."

The interesting point about Alderson's book is that he gives two excellent coloured illustrations of these appearances. From a contemporary review of the book [15] it would appear that he was possibly the first to illustrate these findings in this way.

Baker's Report to the Leeds Board does not deal with treatment, but, in a short note to the Central Board he summarized the methods which he adopted [16]. From this note it would seem that Baker tried most of the accepted or suggested methods of treatment. Brandy and ammonia were very commonly recommended (see Shapter [1] for Exeter), but Baker is more reticent. He says that they are useful up to a point and then detrimental; he adds that

"so difficult is it to know when to stop, that I have relinquished all but capsicum."

This latter remedy, incidentally, is seldom mentioned in contemporary reports. A very common method of treatment at that period was mercurials, especially in the form of large doses of calomel (for example, 20 grains every few hours). Baker had no good results from this method. Transfusion was also in vogue in some places, but he experienced fatal results. The cold-water method was first introduced by Shute of Gloucester [17], and consisted in giving the patient large quantities of cold water to drink. One patient was actually forced to drink seventeen gallons! Baker tried this on two cases, both of which were successful, and he saw it tried on five others, four of which recovered. Treatment by means of the injection of saline fluids into the veins was first practised in cholera by Latta of Leith [18], and in all contemporary reports there is much discussion of the efficacy of the method. Baker reports that he had no success by this means [16]. He also says:

"I have tried injecting saline matter and spirit into the veins, from 8 pints to 14—in no case successfully permanently."

Contemporary confirmation of Baker's findings is given by Richard Birtwhistle [19,] who was deputed by the Skipton Board of Health to visit Leeds and York and see how the cases were treated. Birtwhistle says that the injection of saline solution into the veins was extensively tried in Leeds, but that the method was not found to "answer the sanguine expectations which its first announcement created." He also comments that some recommended abstraction of blood from one arm at the same time that fluid was injected into the other! This "roundabout and swings" conception shows the fundamental errors of the physiology of the period. Birtwhistle's conclusion was that saline injections gave much temporary relief in all cases, but in none did permanent benefit result, and the method was ultimately abandoned in Leeds. In general, the chief methods employed seem to have been those described by Shapter, viz. keeping the patient warm, especially by tins filled with hot water; stimulants such as ammonia and camphor; and the frequent exhibition of calomel (for example, scruple doses every hour). Casson and Horton [20] reported on the treatment of 109 cases in the cholera hospital at Holbeck—which is now a part of Leeds. Their treatment resembled that of Baker, but at the commencement of the disease they gave opium, and they employed large doses of calomel for collapse.

The treatment adopted at York was fully described by Needham [8] and by Anderson [21]. Needham's methods may be summarized as follows; (i) First stage: for diarrhœa, opium (1 gr. to 1½ gr. repeated). Bleeding for headache. If evacuations thin, calomel. Friction, warm applications, mustard emetics for oppression in the chest. (ii) Second stage: Calomel every half hour, with opium. External heat. Mustard emetics in early stage of collapse. Turpentine enemata had been used, but were seldom efficacious. Bleeding was not advised at this stage. (iii) Third stage: A dose of calomel daily. Bleeding may be necessary, "but we do not think that large bleedings can generally be borne," and free application of leeches is generally much safer. Needham comments on the saline treatment recommended by Stevens, that is, the exhibition of non-purgative neutral salts. He did not find the method efficacious; he says that

"in many cases it has either increased the purging or failed to control it."

Anderson's views agree on the whole with those of Needham, but there is a discrepancy regarding intravenous injection of salines. Needham says that thirty cases were injected in York with four recoveries. Anderson says that this method was used in twenty-three cases, of which only five died. He adds that

"if it were of no other use than to give a short time to persons who had not made their wills, &c., that alone would amply repay all the trouble in such circumstances."

At Hull the treatment seems to have been more or less on established lines [6]. Alderson used early venesection, followed by calomel and rhubarb in the first stage. With reference to bleeding, he says that the operation can be performed even when the stage of collapse is impending, provided that there is a good pulse and the evacuations are not profuse. For the stage of collapse itself large mustard plasters or poultices were most successful. For profuse diarrhœa he recommended a lead and opium suppository, and he also tried rectal injections of nitrate of silver with laudanum. He was no blind supporter of the cold-water method. The saline treatment he had tried, but with so little success that he was inclined to attribute any which he had to the *vis medicatrix naturæ*. About this time Ayre of Hull was writing frequently to the medical press about the advantages of minute doses of calomel in cholera [22, 23]. Ayre said that he had treated 191 cases by this method, and of these only 34 died. It was, perhaps, these statements which called forth the following indictment in Alderson's book:

"Mercury and opium ever have been, in all obscure diseases, the sheet anchor of the quack; and on the first appearance of Cholera, when the medical world were alike

unacquainted with its nature and treatment, there was a great disposition to employ them, and particularly mercury, that most severe as well as efficacious remedy. It appears at present that ample experience has brought the practice much into disrepute in Cholera, and although both calomel and opium still continue to be given in all doses, and at all intervals throughout the disease, there are few advocates found for their indiscriminate use."

Favell [24] at Sheffield also tried out Ayre's method, and was not impressed, as we can infer from his question:

"If calomel cures cholera at Hull, how is it that it does not at Sheffield?"

Favell, on the other hand, favoured stimulants and friction of the limbs with flannels dipped in strong liniments. He was an adherent of galvanism, which produced in most cases, he says, decided and immediate improvement.

This is no place to raise anew the stormy history of venesection. Nearly all the medical writings of the period abound with arguments for or against its use, but most authors admit that in cholera it must be employed at least in the early stages of the disease, and nearly all, without exception, are unwilling to oppose the cult of the lancet. I should like, however, to quote a few sentences from a pamphlet by Dickson [25], an Indian army officer who wrote on cholera in 1829. He says:

"Having seen the analogy subsisting betwixt the disease called Cholera and that which takes place in a person who has lost much blood, can we for a moment hesitate as to the proper treatment to be pursued? . . . Many practitioners bleed, blister and stimulate in a breath. Is this either sensible or scientific? If one of these practitioners were called to the bed of a patient who had suffered from hæmorrhage or who had been poisoned by metallic vapours, he would (if he were not previously informed of the cause) draw out his lancet under the idea that the disease was Cholera. This is not prescribing for symptoms but for a name. Ask him why he bleeds in Cholera, he will tell you that it is to relieve cerebral congestion, or to unload the gorged lungs, or to subdue spasms. . . . The lancet then, while it robs the muscles of that diminished energy which constitutes spasm, *weakens the powers of the respiratory muscles also*—and hastens asphyxia. The blood in such a case is the life, and without blood a muscle cannot contract nor a gland secrete. Many die of Cholera who from the first have never suffered from spasm. In the last stage of the disease there is no spasmodic action. The internal parts are palsied and the external strength is laid prostrate. If it be boasted that bleeding has been followed by success, I answer, in those cases that have recovered after venesection, the irritating cause has not been so great, the atmospheric poison has not been so deeply inhaled, and the records of our science bear witness to a successful result in other dangerous diseases where the practice has been confessedly erroneous. If it he proved (which it has been by Magendie) that the action of poisons is favoured by bleeding and retarded by an artificial plethora why should the lancet be resorted to in a disease which has its origin indubitably in an atmospheric poison? The word *poison* is a relative term. It means anything in any shape destructive to the nervous energy constituting animal or vegetable life. Misled by the relations of authors and the encomiums they have passed on the lancet, I gave venesection a trial to an extent which I can never sufficiently regret. Instead of depriving the Patient of his blood I should have been more successful had I transfused blood into his almost empty veins."

These sensible views appear to have passed unnoticed; certainly they were not ventilated or practised in Yorkshire.

The remarks of Baker on ætiology are obscured by the views on the miasmatic theory of infectious diseases which were current in his day. Some of these arguments must have caused the partisans of the contagion theory considerable difficulty. For example, Baker points out that the disease was most prevalent in the low-lying districts of Leeds, especially in those parts where

"from a want cf local cleanliness and ventilation, a malignant state of the atmosphere was likely to obtain."

As has been pointed out, multiple cases in households were not infrequent in these districts. But, says Baker,

"if these distinct attacks upon members of the same family depended entirely upon contagion, how happens it that we so rarely find cases recorded of two persons being attacked in the same habitation situated higher where the miasm does not exist, and where proper attention is paid to cleanliness and ventilation?"

It is obvious that Baker had no idea that the poison might be taken into the system in the drinking water. For example, he mentions that the disease broke out in the first storey of a large building, which had several flats for different families.

"The matter ejected from the patients was thrown down the sink into a sump hole, over which there were persons residing who did not take the disease till this time. Here were then two sources of epidemy—the sump hole and the ejected matter. Under this roof there were 6 cases, 3 deaths."

Thackrah quotes Chapman as stating that

"the grass-cutters of his party were found to suffer severely from Cholera, whilst the rest of the party suffered little. Out of eighteen of these people, five died in three weeks, and as many more were attacked. They were resorting daily to a putrid standing pool, for the purpose of washing their grass. They had themselves connected the attacks with this pool, and of their own accord deserted it, after which no further cases occurred."

Despite many such suggestive incidents, the only writer of the period who seems to have suspected the waterborne theory of cholera was John Parkin [26]. Yet the solution was evidently not far distant, as is evidenced by Baker's statement that

"the cause of an epidemic disease may depend upon the egesta here and there scattered from patients labouring under such complaints, with as much if not more probability than actual contact."

The major portion of Baker's thesis is devoted to the part which filthy domestic conditions and unpaved, uncleansed and unsewered streets played in the spread of cholera. Before approaching this section it will be as well to review what previous steps had been taken to secure a reasonable degree of cleanliness in the town. In 1790 a local Act (30 Geo. 3, chap. 68) was passed

"for better supplying the Town and Neighbourhood of *Leeds*, in the County of *York*, with Water; and for more effectually cleansing the Streets and other Places . . . and removing and preventing Nuisances, Annoyances, Encroachments, and Obstructions therein" [27].

In 1809 an amending Act was passed (49 Geo. 3, chap. 122), and in 1824 an Act (5 Geo. 4, chap. 124) with much wider powers was placed on the statute book. Despite this legislation, conditions in Leeds, as described by Baker, were truly appalling. He shows that about half of the population of the town of Leeds itself (that is, excluding the surrounding townships) lived in streets which were sewered, drained, paved and cleansed. In this half of the town only 245 cases of cholera occurred. On the other hand, in that half of the town in which there was neither common sewerage nor cleansing 1,203 cases occurred. According to Baker, the populations of each of these halves were approximately equal. In three parallel streets, housing about 386 persons, the sanitary conveniences consisted of two small privies, which were in such a state as to be totally unusable. Offensive matter was allowed to accumulate in the unpaved streets. From the privies in Boot-and-Shoe Yard seventy cart-loads of filth—the accumulation of thirty years—were removed by order of the Commissioners. In many streets there was a sump hole—long stagnant—under the flags of every house. Baker's conclusion is that

"if our streets are not properly cleansed, we can hardly expect much cleanliness in either the dwellings, the habits, or the manners of the people."

The Report was presented to the Local Board of Health on January 21, 1833, and that body's third resolution was to the effect that

"as the facts communicated in the said report are applicable to all large towns, this Board is of opinion that a General Act of Parliament for sewering, drainage, cleansing, and paving, would prove a public benefit."

We would expect that the people of Leeds, no less than the population of Britain as a whole, once roused to a white heat of indignation by such enormities, and by the train of death left by the epidemic, would have demanded energetic measures for the "cleansing and purifying" of populous centres. The sequel will be found in a Statistical Report issued in October 1839 by the new Leeds Corporation—which had been formed as the result of the passing of the Municipal Corporations Act in 1835. This Report [28] was the outcome of investigations which extended from November 1838 to October 1839. I have summarized some of the information given in this excellent report, and from this it would appear that there were 586 streets in the town. Of these 247 were classified as "good," 108 as "middling," 135 as "bad," and 96 as "very bad." The authors of this report point out, however, that the designation "good" must be taken with a considerable amount of reservation, since, of the 247 streets which were classified thus, only 70 belonged to the town and were cleansed by scavengers. The old difficulty regarding the shortage of privies had not been remedied. In three adjoining streets, containing a population of 452 persons, there were only two such conveniences, neither of which was fit for use. The streets had become so full of ashes, filth and refuse of every description that their surfaces were far above their original level. The conveniences which did exist were usually situated under archways, and were consequently used by every passer-by.

"Uncleansed because it is nobody's business, and everybody's perquisite, they become offensive in the highest degree."

The Boot-and-Shoe Yard, to which reference has already been made, now contained 340 inhabitants (ten to every house). There were only three privies, *and one of these had not been cleansed since the cholera.* There was no water within a quarter of a mile. In the North-East Ward—in which cholera had been rampant—there were several horrible places which were utterly impassable for filth of the most offensive description. Some important streets were wholly without sewers; many cellar dwellings were never dry; and on the surface of the public way there was frequently a permanent collection of soil and water, "a perpetual nuisance to the eye, and a perpetual fever to the whole body." As an echo of the conclusions of the 1832 Board of Health, the authors of the present Report summed up by saying:

"One thing is certain, that the greater part of the town is in a most filthy condition, which demands an immediate remedy; a remedy which does not seem attainable under any local Act now existing; but calls for an especial enactment, which is doubtless required, not only for Leeds, but, more or less, for every town in the Empire."

It was not until twenty-seven years later, on the appointment of the first Medical Officer of Health for Leeds in 1866, that the necessary sanitary reforms were initiated.

History provides a salutary check to overweening sanguineness. We may point to our modern cities and say, Thus far, and thus, have we travelled in the last hundred years. Yet it should be remembered that in such matters progress should be measured not in terms of actual accomplishments, but rather in relation to those needs which the expert opinion of the time indicates as necessary. There had been abundant evidence before 1832 that the Augean stables of our cities would require a great cleansing; yet, seven years after the catastrophe we find that in Leeds

progress had been non-existent. In the last few years there has been ample evidence that both medical and engineering experts are setting up new standards of communal life. Can the community as a whole rest assured that it is striving to reach these standards?

For the loan of literature relating to this period my thanks are due to Mr. F. J. Boardman, Chief Librarian, Rotherham Public Library, to Mr. R. J. Gordon, Chief Librarian, Leeds City Libraries, and to Mr. J. P. Lamb, Chief Librarian, Sheffield Corporation Libraries.

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Section of Psychiatry

President—DAVID FORSYTH, M.D.

[*December* 11, 1934]

DISCUSSION ON MENTAL HYGIENE—PREVENTIVE MEASURES IN CHILDHOOD

Dr. Susan Isaacs: Before one can frame any principles for practical guidance in early mental hygiene, it is essential to consider what are the processes of growth and development in the mental life. Without a preliminary study of the facts of genetic psychology, including the unconscious mental life as well as the overt behaviour of the child, we cannot hope to arrive at measures that will be preventive of ill-health and unhappiness.

During the last ten or twelve years, the work of Melanie Klein and her colleagues, using in the analysis of very young children the instrument of research created by Freud, has carried our knowledge of early mental development deeper, and made it more adequate to deal with the many-sided facts.

Melanie Klein has shown that the facts of the successive phases of libidinal development, and those sexual wishes of the child towards his parents which are conveniently summed up in the now familiar term "Oedipus complex," are both confirmed and elaborated by early analysis. The interaction of the libidinal wishes, however, with specific impulses of aggression in each pregenital phase, and the interplay of the infant's object-relations in the Oedipus complex with the primitive oral and anal mechanisms of introjection and projection, are both far more complicated than had been realized hitherto.

Each of the pre-genital libidinal zones, particularly the biting phase of oral sexuality, and the successive phases of anal erotism, has characteristic aggressive impulses connected with it, involving specific modes of attack and defence, and specific phantasies. Although genital phenomena appear sporadically, even in the first few months, they are out-weighed in their contribution to the Oedipus complex, and in general psychical importance, by the sadistic pre-genital impulses, throughout the early years.

The pressure of these primitive forms of desire and feeling in the child, from birth onwards, is enormous. His chief task throughout his early years is, not to acquire a series of habits, but to learn by one means or another to control, to modify and to find some satisfactory expression for his instinctual cravings towards his parents.

As a first defence against the primary anxiety of oral frustration and oral aggression during the first six months of life, the infant takes into his own psyche a mother *imago*, or rather two diverse and distinct imagos of the mother, the "good," who yields the bliss of satisfaction in suckling, and removes painful stimuli; and the "bad," who is created out of the experiences of pain and frustration and the child's own impulses of aggression. The "bad" mother does not differ in character from the primitive wish-self of the child, and is endowed with all his own sadism.

This internalized "bad" mother, invested with all the child's own aggressive wishes, gives rise to a vast anxiety. The anxiety of such attacks *from within* leads to an imperative need to project again the sadistic super-ego on to an external parent. In his obstinacies and tantrums the child tests his phantasies of inner danger by real action against the external parents, so as to gain constant reassurance of their power to control him without hurting him, and of their love and willingness to protect him. The night terrors and screaming fits, eating difficulties, phobias, tantrums, and breakdowns in cleanliness, during the second to the fourth or fifth year, all have their deepest psychical roots in this dread of the internalized "bad" parent. In his pleasure-seeking habits, such as thumb-sucking, the child seeks proof of the goodness of those parts of his own body which have been associated with aggressive phantasies, e.g. his mouth in biting. In his dramatic play he externalizes the various aspects of his inner drama and so eases its stress. In his learning, his manifest affections and his growing skills, he gradually builds up a more stable belief in the good parents inside himself, and in his own power of creating and making good, and brings this belief closer to reality.

Even the very young child's relation to his mental environment is thus extraordinarily complex. From at least the end of his first year, his behaviour in any direction is always the outcome of a highly complex internal situation acting in response to real happenings, never of a mere wish or a mere habit. The problem of early mental hygiene thus resolves itself into the question of how to help the child find satisfactory ways out of those intense emotional conflicts which he inevitably experiences during his first three or four years.

I would like to offer certain general suggestions which are the outcome of my own practical experience.

No question more urgently needs ventilation than the psychological factors in the modern practice of infant welfare. The need is great for mothers and nurses and those advising them to recognize the personal and emotional significance of feeding, weaning, and all bodily processes. Only too often the infant is treated as a reflex machine, with a harsh ritual of training in sphincter control which denies him any feelings of his own. It is more than likely that early and rigid training in cleanliness is harmful, since it increases the anxiety both of mother and child. It certainly lessens the pleasure which the mother takes in her child, leading her to expect false standards of achievment, and to be unduly ashamed or afraid of abnormality, if he is not perfectly clean and dry by e.g. ten or twelve months. The use of the word "ought" in public utterances on this point, "the child ought to be clean and dry" by such and such an age, is to be deprecated, since it encourages rigid standards and the fear of abnormality. Routine and regularity are invaluable servants and guides for the mother in her behaviour to the child, but bad masters when dictated to the child, by harsh necessity.

It is thus desirable that mothers and nurses should have appropriate standards, with regard not only to sphincter control, but also to the development of the skills characteristic to the child's age. It is equally unwise to force these virtues upon the child at too early an age, and to deny him opportunity for them at a time when he can achieve them, thus closing the channels of sublimation and ego-development.

Again, it is necessary to recognize individual deviations. Children do not fit—and can never be made to fit—an exact pattern. Even in intellectual development, whilst there is a general sequence, there are marked individual differences in detail, and this is very much more true in social and emotional relations. Every child needs a treatment sufficiently elastic to allow for his personal idiosyncrasies. Whilst it may be true that the normal age for the control of the bladder is, say, two years, it is equally true that a large number of ordinary children will be a good deal later than this, and that if the mother can bear to admit this without feeling it abnormal, she is more likely to aid the child's mental health.

Even under the most favourable conditions, however, crises and difficulties will arise. Such problems as thumb-sucking, dirtiness, nail-biting, phobias, masturbation and night-terrors, will occur in most children, and need specific consideration. The process of teething, the stress of operations and physical illness, of family deaths and partings, will all have to be dealt with from time to time.

I can speak only of one or two of these issues, so as to illustrate the general principle of meeting the child's difficulties with love and skill.

A significant instance is the problem of what to do with a child who cannot bear to be left when put to bed at night. The normal impulse of the warm-hearted mother is to stay and comfort the child. And what does relieve his need is for the mother to stay with him and spend a short time in pleasant talk, not as a concession to his demand, but willingly, and as a part of the regular routine of bed-time, as a natural and pleasant item in their daily intercourse. The need for the presence of the mother is usually only a temporary crisis arising from the child's guilt and anxiety about his own aggression towards her. Her willing love and friendliness reassure and calm him, and presently enable him to fall asleep without her.

Another example is the treatment of nail-biting. A method which I have repeatedly found successful is the application of olive oil to the nails at bed-time, or at any time when the child shows a tendency to bite. This acts, not only because of the physical softening of the nail, which removes irritating sharp corners and fragments, but also, or even mainly, because the mother thus shows that she believes in the possibility of making the nails friendly, agreeable parts of the child's body, instead of sharp, aggressive instruments for scratching and tearing.

Perhaps these will serve as sufficient illustration of the general principle that the ordinary crises occurring with the ordinary child can be successfully dealt with by a positive attitude of love and understanding.

A more general consideration is the wisdom of avoiding as far as possible coincident stresses. Over and over again, one finds, both in actual observation of children and in the reconstruction of early experiences through analysis, that it is when two or more stresses occur together that serious mental disturbance is liable to arise, although each might have been dealt with satisfactorily had it occurred alone. If, for example, there is a death at the time when the child is teething, if he is to have an operation just after he has been naughty, if his mother goes away for a holiday or the new baby arrives after he has happened to be particularly dirty or aggressive, his difficulties will be increased to the breaking point. A very striking sequence was reported to me recently of an aggressive act—biting and kicking—on the part of a small boy, which happened to be followed by the temporary illness of his mother, then an operation on his own tonsils, and within the next month, the birth of a new baby and his being sent to school. It was not surprising that the child regressed to an attitude of whining and clinging babyishness, and total intolerance of any parting from his mother. Of course, such coincidences cannot always be avoided, since we cannot time the teething or the illnesses, or the outbreaks of temper in our children. But in so far as they can be avoided, they should. It is, for example, unhelpful to send a child, without warning, to a nursery school within three days of the birth of a new baby. This happened with one small boy that I know, and resulted in the utmost terrors and despairs.

Another significant instance of this mistake came to my notice a week ago. The weaning of a boy of ten months was begun a fortnight before a complete change of life was about to happen, involving a week's journey from one country to another, and a sea voyage of some days. It was completed within a fortnight of the arrival in the new environment, with the result that the child immediately developed a most violent anxiety and aggression, attacking and biting and bruising himself and other people, and screaming for hours on end in the night. It could be said quite dogmatically that the process of weaning should never be allowed to coincide with

any other important change of circumstance such as this. This is one of those fundamental points where greater knowledge, and a greater gift of imagination and understanding of what these things may mean to the child himself, would be of inestimable value in early mental hygiene. It illustrates, too, the serious error of regarding the child as a reflex machine and underestimating the psychical side of such events as weaning.

There remains the problem of how to deal with the extraordinary crises, and with those children whose anxieties are so great that they are out of the power of the wisest mother to deal with. Experience has shown that not merely hysteria and obsessional neurosis, but psychosis and delinquency can be diagnosed in the child under five years. In these more exceptional instances, the need for early therapy has to be recognized as an essential part of mental hygiene. The work of the child analysts has shown that severe neuroses, asocial development, and psychotic conditions can be relieved and cured, in these early ages, far more readily than in later life.

Where there has been an unavoidable coincidence of stresses in a little child's experience, such as the association of the child's own aggression with the illness of the mother or the birth of a new baby, a prophylactic analysis would, in most cases, be highly desirable.

To sum up, I would suggest the following main desiderata for early mental hygiene:—

(1) A mode of teaching parents which, whilst giving responsible knowledge and skill, will avoid exacerbating their own anxieties.

(2) For the child himself, a background of routine and mild control from infancy onwards, a positive attitude towards the child's attempts to express his instinctual cravings and his phantasies in sublimated forms, and the provision of normal opportunities for positive achievements.

(3) The meeting of the ordinary crises of the child's emotional life with love and positive skill, and the understanding of what weaning, illnesses, partings and deaths may mean to the very young child.

(4) The need for an adequate diagnosis of the more serious difficulties, and—with a not inconsiderable number of children—for an early psycho-analysis.

Dr. William Moodie: The problem of maintaining the mental health of the child may be approached from different directions. We may study healthy individuals and attempt to deduce from their history the reason for their continued health. On the other hand, we may study those who are diseased and try to discover why they have become so. This latter would seem the more productive method because we can to some extent control the correctness of our deductions. We can apply to these diseased individuals remedial measures calculated to counteract the malevolent influences and, if health is restored, we can assume that our reasoning *may* have been correct.

The thoughts which I am going to express in my paper arise from the study of certain children who have in one way or another broken down and shown signs of mental disturbance.

The London Child Guidance Clinic has dealt with over two thousand three hundred cases during the last five years, and in addition the staff have been responsible for the examination of about two thousand children committed to the Remand Home of the London County Council. It is from this clinical material that I shall draw my ideas.

In the Clinic group of cases, treatment of a direct kind has always been applied, calculated to remove or to counteract what was thought to be the disturbing influence, and if the result was successful, the deductions were taken to have been correct. In cases in which deep psychotherapy was also carried out, the direct link was often

found between the fundamental cause and the specific symptoms of personality- or behaviour-disturbance presented. When this occurred it yielded valuable confirmatory evidence. Naturally, since only a small number of the delinquents came subsequently for treatment, the correctness of the deductions could not be controlled—but the results of examination yield some very suggestive figures.

The manifestations of mental breakdown in these children have been very diverse. The symptoms may have been such that the child caused disturbance to the community by violence, habitual stealing, disobedience, temper or bullying. He may have played truant from school or fallen into the hands of the police. Maybe the trouble has been more within himself—he has been nervous, fearful, shy, sensitive, unable to hold his own with others and abnormally imaginative ; or perhaps some special symptom such as nail-biting, thumb-sucking, food-fads or bed-wetting was particularly evident. Many of the children were referred because of school failure—this particular problem taking many forms such as lack of concentration, so-called "word-blindness," inability to calculate or to remember. All the children accepted presented some real problem—and not merely a transient disturbance such as is wont to occur in the career of every normal child. The delinquents had all been sent to the Remand Home through the Juvenile Courts. Many were committed for stealing, for gang activities, for housebreaking or for bag-snatching. A few were there because they were beyond control, and some because they had been found wandering "without visible means of support, and lodging in the open air."

As might be expected, in the Clinic group one frequently found signs suggestive of the neuroses and psychoneuroses of adults. A certain number of children, about 8%, were actually mental defectives, their intelligence quotient being under 70. Some suggested early psychoses. Some children did not appear seriously disturbed but presented a specific educational problem. They were unable to compete with their own age-group although tests of intelligence seemed to show that they ought to be able to do so. Among the delinquents one did not find the same suggestion of neurosis or psychoneurosis. They seemed mostly to be ordinary children. They were somewhat dull in intelligence, and this may be due to the fact of their being a selected group in that they had been caught by the police. At the Clinic one sees a very large number of thieves who have never fallen into the clutches of the law, and probably never will, partly because they are cute enough to get away, and partly because they have been protected by their parents.

This, then, will give a bird's-eye view of the clinical material which we are going to discuss, and the attitude we shall adopt, and we must pass on to some more particular description of just a few of the more important facts which emerge.

The preservation of health can be pursued only by the adoption of wide principles and will always of necessity fail in individual cases where special abnormal conditions exist. There will always be children who are in some way pre-determined to break down, and these will require special management. It seems amply clear, however, that the great majority of children who behave abnormally are inherently sufficiently stable to benefit from the application of some general principles and even to be thereby restored to complete health. How much more then will the application of these principles maintain health.

It stands to reason that, if these children are subjected to a very searching mental analysis, mechanisms will be revealed which are similar to those found in the abnormal adult, and which, even if less marked, can be interpreted as such, but the work of our Clinic has amply shown that in all children one can find, if one's examination is sufficiently deep, all manner of mental mechanisms.

That they are present in pathological combinations and degrees is doubtful.

We all have hearts, if we had not we should not suffer from cardiac disease. They are a necessary evil—so are many mental mechanisms.

By far the most common complaint when children are brought to the Clinic is that they are backward in schoolwork, but examination of every child shows that many more are backward than are credited with backwardness. Actually about 20% are referred on account of backwardness, while examination reveals that about 40% more are sufficiently behind in their work to cause them difficulty and maybe to give rise to problems. This means that about 40% of all the children suffer from educational difficulties which have not been recognized because standardized educational and intelligence tests have not been applied. The ordinary lay estimate of a child's educability is extremely unreliable.

Here I must make it clear that I use the word "backward" in its technical sense—meaning a discrepancy between achievement and ability. A child doing work normal for his life-age is backward if he is markedly above average in intelligence; but a child two years behind in school is not backward if his intelligence is also two years retarded.

There still are many who do not believe in the infallibility of intelligence tests, but this disbelief is generally based upon tests carried out by someone not expert in their interpretation; one cannot expect the local camera-dealer to interpret an X-ray photograph. The intelligence test, in the hands of a competent, skilled, and experienced observer, is an instrument of precision. It does not always give a decisive result, but the skilled worker realizes at once when fallacies occur and can point to the flaw, indicate its cause, and, in doing so, often add greatly to the knowledge of the case.

Every delinquent, and practically every case sent to the Clinic, is given tests of intelligence and also of education.

In something like 60% of the Clinic cases, then, it was found that the child was educationally behind, and to this extent his intelligence was not being utilized. Educational standards were assessed only in reading, writing, and arithmetic, since only such fundamental subjects lend themselves to rating. Clearly such subjects as history or geography will depend on pedagogy rather than on innate capacity.

It was often found that where education was retarded the child presented mental signs and physical symptoms suggesting an anxiety-state. On tracing the history of these conditions, however, it became clear in many cases that the trouble did not commence in anxiety. Many children who appeared superficially to suffer from a neurosis were not originally anxious at all. They had suffered in early life from a mental and nervous tension due to dammed-up mental energy. The young child who is over-active, who is excitable, who cannot go to a party without being a nuisance, who attacks others and is given to temper-tantrums, is very often labouring under a pressure of mental energy which is not being utilized. Such a child eventually becomes anxious; he develops fears, such as of animals, of the dark, of ghosts and imaginary things—but these are only an exaggeration of those dreads which are normal and natural to every child. They are exaggerated because the affective side of his nervous system is hyper-excitable. Naturally, close investigation of his fancies and fears will reveal anxiety-mechanisms in abundance, and, since the majority of such children are of advanced intelligence, they will also give evidence of a precocity of thought in many directions, but to call the state anxiety, and attribute it to deep psychological causes is often wrong.

To allow such a child to run wild is worse than useless. He will, of course, get rid of a certain amount of energy that way, and if we agree with those who believe it is good for a child to behave like a wild animal, then, of course, his behaviour will satisfy us; but if we have decent standards of behaviour we shall find that he does not conform to them. Emotionally and receptively he lives at a higher level—the

ordinary fears of childhood become magnified into terror, control begets temper-tantrums, and annoyance expands into violence against authority.

Anxiety is not the foundation, but under-education. One should make it a practice in dealing with all behaviour problems to investigate the educational situation and, straight away, to adjust it as far as one can. Such subjects as handwork, nature-study, biology, art, and games, do not give this necessary outlet for the energy produced on the intellectual side. Only intellectual subjects will do this, and I have been led to the firm conviction that a great deal of the instability that we find among school children arises in under-education. A vicious circle begins, and besides becoming tense, the child is unable to compete; he becomes worried, he is egged on at home, he may be tutored by an ambitious—yet annoyed and frustrated—father. Feelings in the home become worse and worse, the atmosphere is charged with failure and there is no saying where it will end.

Early and efficient teaching in the fundamental subjects of reading, writing and arithmetic, is the corner-stone of mental hygiene in children, and the remedy is more knowledge as to the value of intelligence and educational tests and less dependence on opinion.

At one time it was thought that many of these apparent anxiety-states in children resulted from inadequate sex-knowledge. This arose from many causes. Undoubtedly there is a tendency to over-emphasize the importance of sex in early years. No one will deny that the investigation of the mind of any child will reveal primitive ideas which are the early beginnings of forces, impulses, and urges which will eventually become components in sex mechanisms, but these are normal to every child and the degree of their alleged association with real sex will depend very greatly on the interpreter. The infant beating the floor may give clear indications to his doting parents of his future as a sculptor, and an analysis in later life may bring retrospective elaboration—not to say falsification—to bear, so that these early primitive, undifferentiated acts come to assume an unreal and unjustified importance and meaning.

My own observation leads me to the belief that interest in sex matters varies indirectly as the standard of educational attainment, and that except in the rare pathological case, the child whose mind is adequately employed, and who is given reasonable security, can be depended on to give little trouble in this direction.

Among the delinquent group backwardness in education was very noticeable. Over 60% of the children were three or more years retarded in arithmetical work, and over 40% were three or more years retarded in reading and writing. We do not yet know what is the exact connexion between this and the delinquency, but it is amply clear in many cases that the delinquency is a compensation for lack of success in school, resulting from backwardness in these subjects. Again, in the prevention of delinquency the education of a child is of paramount importance.

Amongst these backward children, both in the delinquent and in the Clinic group, one finds many who have specific learning difficulties.

The strephosymbolics form the largest class—those who, through an inability to appreciate position and shape, are unable to utilize the written symbol. They fail in reading, writing, and written arithmetic. Their mental arithmetic may be perfectly good and their knowledge of vocabulary and language equally so, but there is this difficulty about the symbol which keeps them back. These children should be carefully combed out and specially taught, if breakdown is to be avoided. Luckily, strephosymbolia usually clears up about the age of 10 or 12, but it has placed the child up till then in a position of inadequacy, unable to read and write, always up against difficulties and never making satisfying progress.

The second factor that seems to loom large behind many of the problems is lack of discipline. I do not here, of course, refer to discipline associated with punishment or suppression, but merely that teaching which gives the child average decent rules

of living. Imagine a motorist entering a large city with no knowledge of traffic lights, or what policemen mean, or which side of the road he must keep, or on which side he must pass other vehicles. He is told that he must find out for himself. Let him experiment. Experience will be good for him.

He does not drive into that traffic with any great feeling of security. On the other hand, if he knows the rules of the road, he will go forward with confidence. It is the same with a child. The child must be taught certain rules for living. He must be guided by the more experienced as to how he should conduct himself. Freedom is all very well up to a point, but to deprive a child of guidance as to how best to tackle life merely leads to insecurity and indecision, and leaves him to make judgments which are too difficult for him and which he cannot really make because his mind is incapable of absorbing and assessing the data upon which he must judge. One finds, naturally, among the delinquents, that discipline in many of the homes has been extremely bad, but one finds this also among the Clinic group of children who show signs of early neurosis or psychoneurosis, especially those resembling anxieties. Many are a prey to indecision and insecurity because they have not been given definite fixed points of conduct from which to start. They have been left to struggle on unaided.

A little girl said to me the other day: "I was protected and at the same time I was allowed to do as I liked, and now when I have to make decisions I find it too difficult. I never decided before, I just did what came into my head at the moment."

In this connexion the child's relationship to the adult is of the greatest importance. The adult should form a base from which the child can work. He should be ready to help the child when difficulties arise, and even to check him when he is running into danger. The parent need by no means be a Barrett of Wimpole Street, but on the other hand, one often encounters present-day parents who are avoiding their proper responsibilities under the pretence of modernity and psychological insight. The remedy here is the spread of reasonable information about the bringing-up of children.

The third cause of breakdown with which I shall deal is a more intangible one. It is a lack of affection and of normal home surroundings. This is, of course, a factor in hygiene which is very hard to alter, because circumstances may make it beyond our control. It is noticeable, however, that children who come from broken homes or homes which have been disturbed by emotional storms between the parents, seem to have had communicated to them an insecurity, a feeling of fear and apprehension, which colours all their attitudes, and gives rise to tensions probably more nearly akin to anxiety even than neglect of intellectual occupation or discipline.

So it is that I would place adequate educational work, reasonable control and guidance, and an undisturbed home life high in the list of preservatives of mental health.

Our considerations of the mental health of childhood must not stop here. There are other aspects, among which physical health is important. The puny child with a bad attitude, flat feet and spinal curvature, is almost sure to develop a mental state with corresponding distortions. Under-nourishment, lack of sleep, fatigue—all these are important. The number of school children whose breath smells of acetone just before a meal, is very large. One feels sure that if greater attention were given to the physical condition and posture of children and their minor metabolic disturbances, their mental attitudes would immeasurably improve.

Another important aspect of mental health must be touched on in closing.

One of the greatest menaces to the child of to-day is parent- and teacher-education of an improper kind. The diffusion of information about mental health is a subject which can be adequately tackled only after much study and in the light of deep knowledge and understanding.

We must realize that in talking to adults about their relationship with children, we shall continually tend to collide with the parental instinct which is strong in every normal adult. Everyone has in him, or her, that tendency to control children and to believe that their minds are as an open book. We were all children once and so "of course" we know how children feel, and above all we understand our own children better than anyone else possibly can!

In spite of this, I have often interviewed parents who have had some abstruse psychological theory given them as the explanation of their children's behaviour. They ask whether their children have death wishes for them, or if they are abnormally sadistic, or whether they are showing a desire for self-punishment. Surely it is bad psychology to teach this kind of thing! Either there are simple common-sense explanations which will appeal to the lay mind if properly and clearly presented, or we must be content to disclose just as much as the layman can accept.

Interpretations in terms of unconscious mechanisms must never be given. This is only logical, since if we believe in repression and that the disturbances which we describe are based on repressed forces, any interpretation of them is bound to arouse only antagonism in our hearer—unless he, being anxious to evade understanding, utilizes our explanation in rationalization.

The most difficult parents are among those who, being inherently unstable, have seized upon psychological theory and become "mental-hygiene-conscious." Very great harm has been done since the War by the widespread propagation of a so-called psychology, which is based on theory alone, and described in a jargon which is only an extravagant verbalization of what was known before. Luckily this phase is passing.

In the wider sphere of the teaching of mental hygiene of children and, as a matter of fact, in all our psychiatric work, do let us remember that we are psychiatrists, and at least try to express our ideas with psychiatric skill. Maybe in so doing we shall have to suppress our pet theories and complexes and talk only as simple folk having a knowledge of human nature, but the result will repay the self-denial, and the progress of our art will be hastened.

Dr. Emanuel Miller: I cannot help feeling that the opposite attitudes adopted by the opening speakers, have introduced into the subject a false dichotomy. While I should personally endorse the views put forward by Dr. Isaacs with regard to the importance of unconscious processes in determining behaviour, I do not think we can entirely discount the effects of breakdown in adaptation on the conscious level. What Dr. Moodie says about reactions to educational difficulties is not to be discounted. The pressure of scholastic demands on the child, the conflicting theories of method in teaching, and the personality-conflicts between teacher and pupil, do produce maladaptations sufficient to cause neurotic symptoms. As long as chronological age, rather than mental age, determines into what educational grade a child shall be placed, reactional behaviour and compensatory mechanism will always be produced in order that the child shall find sure solution. Even if struggles against a hard reality produce regressive behaviour, it does not follow that in all cases it is necessary to start from the bottom in order to correct the evil result. Correction of educational difficulties on the basis of the child's peculiar intellectual endowments may reassert the child's trust in itself. It will allow it to feel that its immediate shortcomings are recognized and it will recognize in the correction a sympathy which gives the child the will to go on. I do not deny, however, that there are many educationally embarrassed children who are backward because of some underlying emotional embarrassment. We all know how some arithmetical and linguistic difficulties can be traced to mental conflicts, but the immediate diagnosis of superficial, as against deep, causes is by no means easy. Perhaps the therapeutic test of educational correction will prove whether or not the

conflict is recent or remote. On Dr. Moodie's findings the therapeutic test has proved, in his estimation, that the disorder of behaviour was determined by the inability to find outlet for intellectual energy.

From my experience of such educationally-retarded children with normal intelligence, there is not always a state of anxiety. Some are indifferent to learning, despite normal intelligence, others are afraid of some subjects—frequently arithmetic. I cannot believe, however, that this is the whole truth of the matter. The variety of symptoms, the various behaviour-disorders, indicate some personality-factors which only some analysis could disclose. My own experience of six hundred cases at the East London Child Guidance Clinic, and two hundred at the West End Hospital do show the effects on behaviour of educational stresses. But from time to time the complex clinical picture was striking, and correction of educational difficulties did not lead to improvement in all cases of backwardness of Dr. Moodie's type. Moreover we must ask ourselves whether Child Guidance Units do not tend to get this type of case because of the large number sent from schools. Of a series of six hundred cases, two hundred came from school doctors and seventy-four from care committees. These are children who frustrate the teacher's purpose in one way or another.

What of the large number of cases which come from other sources—or could come from other sources—particularly from doctors? On investigation we found that most cases came at the ages when school medical examinations took place, namely 5, 8, and 13½, indicating what a selected sample we have. Of 454 cases, 179 came from these age-groups alone, the rest from all other ages between 1 and 17.

I think, therefore, that in such Child Guidance Units we tend to have a selected group, and many neurotic disturbances are not seen at all. Of course we see some—quite a large number—but the dice are loaded.

A case can be quoted of a boy who was educationally retarded, but who proved to have an intelligence quotient of 109. He frequently played truant from school. The relationship between boy and father was in question, and in one teacher he obviously saw a father-image. He improved after removal to another class, but the truancy has continued. Social adjustment has not helped so far. There is no doubt that there exists an emotional conflict which requires further elucidation.

I quote this subject, because it has some bearing on therapeutic method and therapeutic success. Given a large number of educational cases, and cases from school sources, we incline to methods which are necessarily surface ones; deep therapy is not needed.

Some form of deep therapy is needed in the cases of psychoneurosis and behaviour-disorders uncomplicated by backwardness and specific educational maladjustment. The methods of therapy—psycho-analysis of play, drawing, and dreams—have thrown much illumination on child neurosis, too valuable to be spurned because of its strangeness.

Many cures have been registered by these approaches, but it is rarely possible to get good results in Child Guidance Units, because of the large number of patients and the small number of attendances. How much suggestion works in these cases we cannot say, unless we study for a long time the after-effects of child analysis. What we can and must do is to apply prophylactic methods to arrest neurotic reactions. In this respect I am in full accord with Dr. Susan Isaacs. To this must be added psychotherapy for these maladjusted persons who are thinking about marriage. Not only must we forestall the dangers arising from pregenital fixation in children, but we have to consider those mental peculiarities in fathers and mothers who use these children unconsciously to solve their psychological problems.

Lastly, a neglected field of therapy in children is the observation of children in group-play. Not only can we observe much of the social life of children in this vital situation, but winning neurotic children back into the social world of those of their own age is much more important than getting them to acquiesce in the social life of adults. Asociality in children is sometimes a cause of difficulties in school, and a healthy attitude to group-life may be more important in some cases than failure to use up intellectual energy.

Dr. Mildred Creak commenting on the stress laid by Dr. Isaacs on the variations among individual children, pointed out that once this factor of periodic stresses was accepted, the concern of parents and teachers, who might themselves feel responsible, would be lessened, greatly to the benefit of the child.

She was glad that Dr. Moodie had made so clear the educational factors in maladjustment. During the investigation, at the Maudsley Hospital, of groups of children with reading disabilities or arithmetic difficulties, certain features were beginning to emerge with some clarity. As a rule, one or other of these subjects seemed to be the stumbling-block, while in a few cases there appeared to be a general inhibition towards all learning, in spite of good intelligence. The latter group rarely failed to show an emotional cause for this attitude, but in the others very often the sense of failure, or a super-added anxiety giving rise to truancy and other forms of behaviour-disorder, were secondary to a highly specific disability. Some of the cases almost fell into the category of word-blindness although, in her experience, these were rare. With more interest being shown in these cases, it should become possible to anticipate the onset, say, of a reading disability. Thus earlier recognition, and individual treatment and re-education might then do much to alleviate the discouragement of both child and teacher.

Dr. Noel Burke congratulated Dr. Isaacs on proceeding from theory to simple practical advice which could be interpreted as "don't fuss," "don't make unnecessary crimes," "don't be self-centred in your dealings with the child."

It was not always easy, even for a trained parent, to carry out this advice in real life, but the essential in the mental hygiene of children was to teach or treat the parents. This had been his experience in the East London Child Guidance Clinic and he disagreed with Dr. Moodie's view of the greater importance of educational mistakes. Educational difficulties were often due to emotional stresses in the child's mind and not to the methods of the teacher.

He further called attention to the importance, in this subject, of considering the innate nature of the child himself, because it was this which decided different kinds of response to very simple environmental experiences.

Dr. Margaret Lowenfeld said that she wished to associate herself with Dr. Moodie in regard to the importance of the intellectual factor in the production of unsatisfactory mental states. Dr. Moodie had pointed out the large part played in children's maladaptations by the unused intellectual energy. In the work of the Institute of Child Psychology she and her colleagues had been particularly interested in the operation of this factor in very young children. She would like to draw attention to two facts.

(1) The work of Professor Charlotte Bühler on the relation of the type of apparatus provided for learning in small children and their capacity to learn. She felt that far too little attention was paid in this country to the scaffolding of early education.

(2) The supreme importance of the emotional factor in securing for a child its maximum intellectual output. Without a knowledge of the child's emotional attitude to knowledge it was often impossible to rectify his failures in this direction.

No one could learn unless they wished to learn, and what was needed was a much wider and more intimate knowledge of the motives that lay behind learning and the emotions that made learning possible. [Illustrative cases were quoted.]

The President said that if there was one fact arising out of the discussion which deserved to be stressed more than any other, it was that the first five or six years of life were decisive in the matter of mental health, and within that limit of age, the first year counted for most, the second more than the third, and so on.

Section of Physical Medicine

President—J. Barnes Burt, M.D.

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Rapid Rhythmical Movements an Alternative to Osteopathic Manipulations for the Cure of Back Pain

By T. Stacey Wilson, M.D., F.R.C.P.

In the first place I wish to say that I fully recognize the value of joint manipulation such as that taught by osteopathy for the cure of back pain. Moreover I think the assertion may truthfully be made that if the medical profession had recognized the success in the treatment of back pain by manipulation which was attained fifty years ago by such men as Hutton, manipulation of the spine would have long ago become one of the ordinary methods of treatment. The result of this would have been that one of the chief reasons for the existence of osteopathic practitioners would have ceased to be operative and we should not now be threatened with their registration as an organized profession.

Two physiological principles are, I believe, concerned in cases in which pains in the back and elsewhere are curable by manipulation. They can be expressed by the following propositions which may, I think, be accepted as aphorisms :—

(1) Injury to a joint or to the muscles associated with it usually results in the fixation of that joint by involuntary muscular activity, in order that recovery may be facilitated.

(2) When once involuntary muscular activity has been originated for the purpose of fixing a joint, it is liable to persist as a " habit " phenomenon for months, or even years, after the need for fixation of the joint has ceased. This is true more especially of joints such as those of the spine where voluntary movement does not play a prominent part in the activities of the joint. This persistent fixation of joints is liable to give rise to pain or other symptoms.

To these two propositions a third may be added :—

(3) Osteopathic manipulation is a very effective method of arresting " habit fixation " of joints and curing the patient of the longstanding pain or other symptoms due to it.

Something further must now be said as to these propositions: In the first place where the spine is concerned, a sudden muscular fixation of a joint may prove detrimental to recovery instead of favouring it.

Owing to the complicated character of an intervertebral joint, sudden strain or injury may cause a slight displacement of bony surfaces or fibrous structures and a sudden fixation of the joint will prevent such structures from resuming their normal relationships. A slight displacement of this nature is, in osteopathic terminology, described as a subluxation.

The chief object of this communication, however, is to introduce to you a fourth proposition in addition to the three already given :—

(4) A special type of muscular exercise which consists in rhythmical to-and-fro movements having a rapidity of eight complete movements in each five seconds, is capable of dominating involuntary muscular activity and counteracting "habit fixation" of joints.

The great value of these movements lies in the fact that by their means most cases in which back pain and other symptoms are due to "habit fixation" of the spinal joints, can be cured by any medical practitioner without having to seek the assistance of some skilled manipulator.

Where however the skilled man is available and the patient able to pay, the cure is a more rapid and a simpler one than where the patient has to practise exercises daily for perhaps many weeks.

In another type of case also, the help of a trained manipulator is desirable, namely, where, owing to a neurasthenic condition, the patient's nervous energy is at a low ebb, and the practising of movements is therefore unduly burdensome.

These special exercises were first used by me at the 1st Birmingham War Hospital for the treatment of three soldiers who were suffering from incapacitating back pain, owing to having been blown into the air by shell explosions. As War-Office regulations did not admit of my obtaining osteopathic treatment for them, and as I knew that other types of involuntary spasm, such as trade spasm, yielded to rapid rhythmical movements[1] I devised the special exercises described below and found that they were as efficacious as osteopathic manipulation would have been, and cured the patients in a few weeks.

During the last seventeen years I have found these exercises of great value for the treatment of patients in whom back pain was associated with deficient mobility of certain intervertebral joints and, by means of them, I have cured patients who otherwise would have needed osteopathic manipulations. The following is a remarkable case of this nature.

Miss L., aged 68, consulted me for pain of supposed gastric origin, loss of weight, and general ill-health in part due to the very limited amount of food she was taking. The presence of pain in the fifth and sixth interspaces on the right side as well as on the left, suggested a spinal origin rather than a gastric one, and on examination there was found to be such immobility of the intervertebral joints that when the patient was fully bent forward the only visible spinous processes in the dorsal region were those of the fifth and sixth vertebræ, which were very prominent —and that of the seventh which was just visible. The spinous process of the second lumbar vertebra was prominent, but those of the first lumbar and the lower dorsal vertebræ were not visible. The pain and general ill-health were clearly due to the abnormal condition of the spine.

[1] "On the value of rhythmical exercises for the cure of spasmodic neurosis," *Brit. Med. Journ.*, 1907 (ii), 133.

The patient was taught how to practise the exercises and she performed them several times each day. When next seen, at the end of nine weeks, she was greatly improved, and after three months of treatment she called to report that she was cured. Appetite and digestion were normal, and she was free from all pain. On examination, it was found that the mobility of the vertebræ had been completely restored, and that all the dorsal spines maintained their normal relationships on movements of the spine.

The next case is of extreme interest because it shows that a case of longstanding pain due to "habit" fixation of muscles can be as suddenly and completely cured by these exercises as it can be by osteopathic manipulations.

The patient, a woman, aged 36, consulted me on account of severe—and, at times, incapacitating—pain in her neck and left shoulder from which she had suffered for the last nine years. The pain was originated by a severe strain of the left shoulder, the result of being picked up by her left arm during a fainting attack, by a woman, who carried her for about 200 yards slung over her back like a sack of corn. At the time she was on the verge of a nervous breakdown from overwork as a nurse in a hilly district of South Africa, and was ill for six months afterwards with severe pain in the neck and shoulder. She states that the part played by the strain was not recognized and the pain was thought to be a symptom of her neurasthenia.

She returned to England and twelve months later was married. At this time she had more or less constant pain in the neck and shoulder, liable to become severe on exertion unless she was very careful. She suffered from two types of pain: Firstly a dragging pain of a rheumatic type in the shoulder-muscles, which was aggravated by continuous use of the muscles and from which she was never entirely free. This pain was associated with a dropping of the left shoulder below the level of the right, and relief was given by supporting the left elbow in some way. When standing or walking she would often support the left elbow with the right hand.

The second type of pain from which she had suffered more or less for the last nine years was a deep-seated pain of considerable severity in the muscles of the neck. This pain would be brought on by actions which involved an elevation of the shoulders when the head and neck were bent forwards. When once this pain was originated by some action of this type it was liable to persist for several weeks, or even months, at first being so severe that—to use her own words—any movement of the head or neck would make her groan.

Both types of pain have been less troublesome of recent years; she has never been free from the dragging pain and has been liable to attacks of the deep-seated pain. The last one of these was brought on in August 1934, when teaching her daughter to swim, and she was not quite free from it when she saw me at the end of September.

My investigation of her shoulder and search for fibrositic nodules caused a sudden increase of this pain. I immediately gave her a series of rapid rhythmic movements of her head laterally and forwards and backwards. After only eight to-and-fro movements in each of the four directions, she exclaimed, with delighted surprise in her voice, that the deep pain had entirely gone. I then showed her a series of similar movements for the shoulders and helped her to make them, and in a few minutes she found that her left shoulder was free from all pain on movement. She was subsequently able to keep herself entirely free from pain by occasionally practising the exercises.

Reviewing this case: The dragging pain in the shoulder must have been due to habit fixation of some of the muscles, otherwise it would not have been so rapidly and completely cured by the exercises.

The cure of my own neck-pain by a little osteopathic manipulation enables me to understand the possibility that a similar but very severe pain may be curable by rapid rhythmical movements.

With regard to the rapid and rhythmical exercises the following points must be noted:—

(1) The movement must be a voluntary muscular movement by the patient.

(2) The movement must be a to-and-fro one calculated to influence muscles which are presumed to be in a state of involuntary fixation or are known to be unduly rigid because pain results from movements which exert traction on them.

(3) The movements must be rapid. In the case of the spine at least eight complete to-and-fro movements must be made in each five seconds.

(4) The movement must not consist of two equal parts, so far as the vigour put into it is concerned. The first half must be forcible and sudden so as to stretch the resisting muscles as much as possible (short of causing undue pain) and the return half must be gentle and free from effort.

(5) Eight consecutive movements are found to be a convenient number. In order to ensure rhythm and due rapidity it is well to make the patient count aloud as each movement is done. Also it is helpful if the number is called as the maximal effort is made at the end of the first half of the movement.

The following three types of exercise are what I have found effective in restoring mobility to immobile intervertebral joints. In all three the patient does the exercise while seated so as to fix the pelvis.

In the first the patient sits as erect as possible, with the arms folded on the chest and rotates the head and body as a whole round a vertical axis running from the vertex to the sacrum. There must be no special differential movement of the head, but when the body is swung round (say to the right) the head will naturally turn further round than the shoulders do, and the shoulders than the lower part of the body. This movement brings equally into play all the spinal muscles from the neck to the sacrum.

For the second movement the patient sits with the arms folded on the chest. The rotating movements of the head and shoulders are then made round an axis which nearly approaches the horizontal. To start with the patient is looking at the floor. At the end of the upward rotation to right or to left he is looking up at the ceiling. This exercise specially affects the spinal joints in the lower dorsal region.

The third exercise is calculated to influence the joints of the neck and the upper dorsal region. In making it the patient sits in a low-backed chair with the arms folded and anchors himself by hooking his toes round the front legs of the chair. He then forcibly throws the head and shoulders backwards and to the right as if making an effort to look at the floor behind and to the right of his chair. He then makes a similar series to the left.

Modifications of these movements may be found to be desirable for special cases.

I believe that a principle of very far-reaching importance is involved in the cure of back pain such as I have described by these movements, and it will probably be found that other types of persistent muscular pain are curable by them, such for example, as the pain of the less severe types of lumbago and of tennis elbow.

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Photo-Dynamic Sensitization : Biological Action and Therapeutic Application

By Albert Eidinow, M.B.

Definition of photo-dynamic sensitization.—Photo-dynamic sensitization may be defined as the mechanism by which the chemical composition of living cells may be altered following their exposure to rays of light, which normally in themselves have no specific chemical or biological action. Experimentally it is possible to sensitize living cells to infra-red, luminous, ultra-violet rays and X-rays by the use of selected specific chemical substances, such as metallic salts, organic dye-stuffs, etc., known as light sensitizers.

This mechanism is similar to the method employed in sensitizing photographic plates. The use of oxyquinoline and cyanine dyes has made it now possible to obtain photographs by exposure of films to infra-red rays, and the results obtained are similar to those previously obtained following their exposure to the ordinary visible rays of the solar spectrum, and are even more striking. During the past years I have performed experiments by which it has been possible to sensitize bacteria, unicellular organisms, blood corpuscles, etc., to either infra-red, visible, or long ultra-violet rays. The detail of much of the work has already been published in the *British Journal of Radiology*, 1930, iii, p. 113 seq. My conclusions from these investigations showed that direct bactericidal action and damage of blood-corpuscles, tissue cells, etc., resulted, provided that they were irradiated in suitable media which was free from proteins. The biological action of all light sensitizers was controlled by: (1) The volume of fluid suspension irradiated; (2) the intensity of the source of light rays; (3) the length of exposure and the distance from the source of irradiation; (4) the temperature; and (5) the concentration of chemical sensitizer present.

Selective action for each group of rays, from the infra-red to the long ultra-violet region of the spectrum, was obtained by suitable choice of sensitizer. Further, the secondary radiations or fluorescent rays excited by exposure of chemical substances to X-rays or long ultra-violet rays were of sufficient intensity to cause biological reaction. In living animals two degrees of reaction were obtained. Large doses of sensitizer and intensive irradiation caused death of animals from "acute light stroke"; smaller dosage and weaker irradiation produced mild local and general reactions. The latter could be applied for therapeutic measures, and the dosage controlling these two reactions can be determined by preliminary test in vitro, by studying the hæmolysing power of the sensitizer employed on a 2% suspension of red blood-corpuscles in saline. Thus with eosin, a concentration of 1 : 100,000 = 10 mgm. per kilogramme weight, will cause mild therapeutic sensitization, but stronger doses—1 : 10,000 to 1 : 30,000—may cause death of the animal after exposure to a powerful source of visible rays. The use of chemical sensitizers gives intensified and prolonged reactions similar to ultra-violet irradiation but penetrating to a deeper zone through the skin and subcutaneous tissue.

From these observations it has been shown that all tissue cells which are sensitive to ultra-violet rays may be made sensitive to luminous rays by means of certain suitable chemical compounds known as light-sensitizers. Many of these compounds have affinity for the serum proteins and in this way inhibit photo-dynamic action in vitro but not in vivo. After union between the tissue cell and the sensitizer has occurred, the luminous rays produce reactions which are similar to ultra-violet irradiation, but this takes place at a deeper level and therefore

produces reaction of greater severity. Many of the sensitizers are readily soluble and are rapidly excreted. Sensitization can only occur during the period when sufficient concentration of sensitizer is present within the tissues irradiated, and combined with the living tissue cells or tissue fluids.

The action of light rays on the normal skin.—The normal white skin absorbs and reflects infra-red, luminous and ultra-violet rays. The absorption of rays of light by the skin is the method by which radiant energy acts on the human body, and it may be stated that the metabolism of light occurs in the normal skin. The degree of penetration and reflection varies in different parts of the body and is different for each individual wave-length of light. The long infra-red rays are absorbed by the most superficial skin layers, the short infra-red, orange, and yellow rays penetrate deeply through the skin to the blood-vessels and underlying subcutaneous tissue. Sonne has shown that the short infra-red and luminous rays can heat the tissues at 0·5 cm. depth from the skin surface to 47·5° C., and he found that this temperature was 5° C. higher than that of the skin surface. The blue-violet luminous rays do not penetrate beyond 20 mm., and are mostly absorbed by the hæmoglobin in the superficial blood capillaries. The longer ultra-violet are totally absorbed in the surface layers of the skin and cause a bluish-green fluorescence of the normal white skin. Ultra-violet rays of wave-length shorter than 3100 A.U. are absorbed by living epithelial cells and excite photo-biochemical reactions which cause latent erythematous reactions, and other biological actions, such as vasodilatation, intradermal and subdermal polymorphonuclear leucocytosis and the activation of vitamin D from ergosterol present in the lipoid substances of the skin cells and secretory glands. The intensity of erythema produced by irradiation of the skin with light sources emitting ultra-violet rays of wave-length shorter than 3,100 A.U. varies with the depth of pigmentation present, the thickness of the horny layers of epidermis consisting of dead or predesquamated skin cells, and the fat content of the skin. The condition of the local circulation and the temperature of the skin at the time of irradiation influence erythema reactions. The age of the skin cells plays a considerable part, for the skin is a rapidly regenerating organ, and as the chemical nature of the skin cells alters with age, they become more opaque to ultra-violet rays and therefore lessen the degree of erythema reactions. In childhood ultra-violet erythema reaction cannot be normally demonstrated until the second or third year of life. In the aged, the skin is hypersensitive to irradiation. Conditions of severe anæmia and ill-health weaken the reaction of the skin cells to ultra-violet irradiation.

Under normal conditions the infra-red and luminous rays have only a transient action on the normal skin; these rays are absorbed or reflected by the epidermal cells and heat is conducted to the circulatory blood-vessels and deeper structures. Excessive absorption of heat will naturally cause blistering and necrosis of the irradiated tissues. The blood-vessels show an immediate response, vasodilatation and an irregular area of skin erythema being produced. After the cessation of irradiation this reaction gradually subsides and the tissues return to the normal state.

The increased blood circulation of the irradiated skin can be demonstrated many months after ultra-violet irradiation, for if 0·01 grm. of histamine is injected subcutaneously, the portion of skin which has received ultra-violet irradiation will stand out and show a bright red flushed area in contrast to the normal non-irradiated skin.

Light pigmentation may occur either after the single application of an erythema dose of ultra-violet rays or may result from repeated applications of weaker ultra-violet irradiation, which does not cause visible skin erythema. In the early phases pigmentation is produced by the displacement of pigment from the deeper skin cells to the surface. Later, with the regeneration of the skin cells, pigment is found in the

basal epidermal cells. The capacity of the skin to develop pigment varies with the hereditary nature of the skin cells; brunettes, as a rule, pigment more strongly and more rapidly than blondes. The different regions of the skin react with unequal intensity; the naturally darker pigmented areas of the skin cause stronger pigment reaction to ultra-violet irradiation. Pigmentation is a chemical process and originates through the action of a ferment, an oxidase, present in the epithelial cells, acting on a colourless precursor of the skin pigment melanin, dioxyphenylalanin. The irradiation of the skin increases the activity of the oxidase ferment and changes dioxyphenylalanin to melanin. In cases of vitiligo and leucoderma this pigment reaction is absent, although these skin areas are often more sensitive than the normal skin to ultra-violet irradiation. It has been suggested that the ultra-violet rays which cause erythema of the skin are not necessarily of the same wave-length as the pigment-forming rays. The nature, intensity, and colour of the pigment found in the skin varies with the intensity and nature of the source of ultra-violet rays which is employed.

Freckles.—The pigmentation of the skin protects mostly against the effects of heat, infra-red rays and luminous rays. Melanin strongly reflects and absorbs infra-red and luminous rays and in this way prevents their deeper penetration, protects against over-heating of the deeper tissues and blood-vessels, and guards the body against heat and light stroke.

The development of pigment also acclimatizes the skin and immunizes it to some degree against the erythema action of ultra-violet rays. In addition to this the hyperplasia of the epidermal cells and increased vasodilatation of blood capillaries screens and protects the deeper dermal structures from harmful effects of excessive exposure and absorption of ultra-violet rays. During the early stages following the application of ultra-violet rays the hyperæmia, the exudation of lymph, dead epidermal cells and local leucocytosis screens off and protects the skin, so much so that at this stage the skin is immune for the action of ultra-violet rays. This effect persists until the erythema reaction subsides and the irradiated epidermal cells desquamate and ultra-violet rays can now penetrate to the new living young skin cells and again the erythema response to irradiation can be produced.

The action of light rays on skin pathologically sensitive.—There are relatively very few instances in which the skin is abnormally sensitive to light. The presence of a light-sensitizing substance within the body tissues may occur as a hereditary and congenital metabolic disease, or such substances may be accidentally administered or may be formed by abnormal products of metabolism and cause a temporary pathological condition of light-sensitization. Apart from xeroderma pigmentosum, disease due to abnormal sensitivity to ultra-violet rays is practically unknown. Intensive erythema reactions of the skin following solar or therapeutic irradiation are often stated to be due to hypersensitivity to ultra-violet rays, but careful analysis of facts will often reveal a logical explanation. Similarly there is little proof of abnormal reaction following the application of infra-red rays.

Skin diseases following exposure to light are due to the presence of abnormal photo-dynamic substances in the tissues. The exposure to the visible rays excites photo-biochemical reactions in the skin and the production of toxic substances which may cause local and generalized lesions.

Acute Diseases of Skin following Exposure to Light

Hydroa æstivale or vacciniforme.—This is a congenital and hereditary skin disease occurring in childhood and persisting for many years. In this condition skin lesions appear on the areas of skin exposed to sunlight. The onset of the lesions occurs during the early months of spring and the lesions greatly diminish if the skin is protected from the rays of light. The presence of uroporphyrin and coproporphyrin,

in the urine and fæces, respectively, has shown that there is an endogenous type of light-sensitization disease due to the presence of a photo-dynamic substance similar to hæmatoporphyrin. The blue-violet visible rays aggravate the skin lesions as the greater sensitivity of the porphyrins occurs with these rays of light.

Chronic polymorphic light diseases.—In 1878 Hutchinson described skin lesions which he called summer prurigo, prurigo æstivale, summer acne. These lesions appear in the spring and summer, recurring several years in succession, and completely disappear during the winter months. They are similar to those in hydroa vacciniformis and to conditions of eczema solare described by Veiel in 1887.

Haxthausen has classified 30 cases, and his observations carried out over a period of many years have shown that an eczematous type of rash or a papular eruption may occur alternately in the same patient. These lesions are common in women, usually occurring in blondes with poor power of pigmentation, but they have been described in brunettes with well-pigmented skins. Hereditary disposition has been demonstrated. The onset of these lesions is commonest after the onset of puberty, but skin lesions occurring in early childhood or later in life at the age of thirty are known. The rash is confined to the areas of skin exposed to light,—the skin of the face, dorsal and radial sides of the hands, and the forearms, neck and the upper chest wall. The nose, cheeks and forehead are mostly involved. Itching and irritation of the skin is the prominent symptom; this is followed by the appearance of a diffuse erythematous rash with exfoliation and desquamation of the skin. At times seropapular eruptions are seen. The lymphatic glands of the neck and supraclavicular areas are enlarged. Examination of blood, urine, and fæces fails to demonstrate abnormal pigments; uroporphyrin and coroporphyrin are absent. Barber and Howitt have described changes in the bacterial flora of the fæces, associated with indicanuria and gastric achylia.

There is no specific treatment for these lesions; protection against the luminous rays of the sun is the safest palliative measure. Hutchinson and Rasch have seen amelioration after the administration of arsenic. Calcium chloride and calcium gluconate appear to lessen the irritation symptoms and itching of the skin.

The investigation of the reaction of the skin of these patients to light, showed that exposure to orange, yellow, and green rays produced an erythematous wheal which itched and irritated directly after exposure. The addition of infra-red rays accelerated and aggravated these lesions. This skin lesion persisted for two or three hours and gradually subsided and disappeared. The reaction to ultra-violet rays showed normal response; an erythema occurred with the same intensity of radiation as that which would cause similar reaction in the normal white skin. The skin which had been exposed previously to ultra-violet rays and showed an erythema reaction, appeared to be much less sensitive to the action of the visible rays and did not evince so much irritation and itching or the production of a raised urticarial wheal when exposed to the same source of luminous rays.

Following the exposure of the skin to ultra-violet rays, an area of skin could in this way be protected to some extent for from ten to twelve days, but after this period, the irradiated area again showed abnormal sensitivity to the luminous rays.

The examination of the red blood-corpuscles, blood serum, urine, and fæces has generally failed to demonstrate clearly the presence of a photo-dynamic sensitizing substance. Haxthausen has stated that the intracutaneous injection of the blood-serum of patients suffering from chronic polymorphic light disease of the skin will produce a red raised itching wheal at the site of the injection. My attempts to immunize against the irritative action of light have failed. The repeated intramuscular or intravenous injection of 10 c.c. of the patient's own blood or blood-serum exposed to the air-cooled mercury-vapour lamp has failed to alter the abnormal skin reaction. I have now employed a paraffin-wax preparation made by

mixing tannic acid 1 : 1,000, mercury, biniodide or creosote 1 : 10,000, chloretone 1 : 20, dissolved in paraffin-wax melting at 115° F. It is important to ensure this melting point of the wax. This preparation can be tinted by means of carmine, finely powdered charcoal, indian ink or powdered chalk, to match the natural colouring of the patch of skin. It is melted in a water-bath and applied in a thin mask, and remains for twenty-four to forty-eight hours.

Pellagra.—Pellagra is a disease characterized by dermatitis, gastro-intestinal disturbances, and lesions in the central nervous system. It is believed to be due to a deficiency of vitamin B_2 in diet and is associated with diets rich in maize and poor in meat and milk. The skin lesions generally occur in the early months of spring. Diffuse symmetrical areas of erythema of the skin occur, followed by desquamation, pigmentation, and, later, atrophy. The skin erythema, however, also occurs on parts of the skin not exposed to sunlight. Further, it is often seen in pigmented skin of negroes, but as a rule the lesions became aggravated by exposure to sunlight. Hausmann is of the opinion that there is no relationship between these skin lesions and the exposure to sunlight, but Aschoff suggests that the skin lesions are due to optical sensitization caused by bad maize. Jobling and Arnold state that pellagra is not a vitamin-deficiency disease, but is due to intoxication by a fungus, producing fluorescent substances which act as photo-dynamic sensitizers. They isolated this fungus from the fæces of cases of pellagra and showed that ethereal or ethylacetate extracts of this fungus would cause photo-dynamic reaction in inoculated white mice and were lethal to paramecia when exposed to light. Guinea-pigs fed on a diet of maize for long periods show necrotic skin lesions of the ears and other areas and may die when exposed to light, but recover when kept in the dark. The presence of a similar fungus in bad maize would possibly correlate this condition.

A well-balanced diet, containing a high protein content, aids recovery, but the experimental exposure to sunlight during the course of the disease produced a typical pellagra dermatitis. Attempts to extract photo-dynamic substances from the fæces, urine, and blood have so far failed. This may be due to the small quantity of photo-dynamic substances present and difficulty in demonstrating its presence by biological means unless a sufficiently high concentration of sensitizer is present.

Unclassified dermatoses due to abnormalities of metabolism.—Pulay has described exfoliative dermatitis and eczematous rashes occurring after exposing the skin of patients who have a uric-acid diathesis or hyperglycæmia. Howitt and Barber suggest that abnormal products of metabolism may act as light sensitizers. In such cases the predominance of streptococci in the fæces is often found. I have been able to show that some of these streptococci and some of the lactose-fermenting coliform bacilli grown on blood-agar slopes suspended in saline and in broth can be at times proved to contain photo-dynamic substances which will rapidly hæmolyse a suspension of red blood-corpuscles in saline, or destroy paramecia when exposed to the visible rays of the mercury-vapour lamp, filtered through a screen of window-glass 3 mm. thick.

Xeroderma pigmentosum.—This skin lesion was first described by Kaposi in 1870. It is a very rare hereditary abnormal reaction of the skin to light, which causes scattered pigmented plaques, scar tissue, atrophic skin lesions, telangiectases, and malignant warty papillomata. It is more common amongst blondes.

The onset of the disease occurs in childhood with the development of an intensive erythema on the exposed areas of the skin, following a feeble exposure to the sun. This erythema takes a long time to disappear, much longer than normal, and is followed by a deep pigmentation. The pigment, histologically, can be seen to spread from the superficial to the deeper skin cells, and is of the melanotic type. Areas of atrophic skin, with hyperkeratosis, fibrosis, and loss of elastic fibres and collagen, appear in irregular areas of the irradiated skin. The condition declines somewhat in the

winter months and recurs in the spring and summer. Later in life areas of telangiectasis appear in the atrophic and fibrotic skin area, and warty nodules, which spread and multiply, invade the pigmented areas. These tumours are mostly basal-cell melanotic carcinomata, but adenocarcinomata and melanotic sarcoma and endotheliomata have been described. The disease is usually fatal. No evidence of photo-dynamic substances could be obtained from examination of the blood, urine, or fæces. This appears to be a condition of increased sensitivity to ultra-violet rays and abnormal reaction of defence and protection.

Analogous to this, is the condition of "sailors' skin," xeroderma pigmentosum tarvidum. The areas of skin exposed to light, later in middle age (about 50 years), become bluish-red in colour, thicken, and are covered with warty growths. Farmers, postmen, sailors, and many people who are habitually exposed to open air and sun, are affected. These warty growths later develop into malignant tumours. Hyde has demonstrated the frequent localization of skin cancer on areas frequently exposed to light, and the rarity of these lesions in the pigmented skin of negroes.

Bernhard, however, has pointed out that although the condition of sailors' skin can be seen in many who are constantly exposed to the sun of the Swiss Alps, i.e. guides, etc., he has never seen a case of skin cancer on the face or hands of such persons. The association with tar or tar cancer may possibly explain the malignant changes in sailors' skins. Putschar and Holtz claim to have produced skin cancer experimentally by prolonged exposure of rats to the rays of the quartz mercury-vapour lamp.

Skin diseases aggravated by exposure to light. Vaccinia: It has been claimed by Finsen and his co-workers that ultra-violet rays are irritant to the normal skin and therefore would aggravate the healing of the pustules of variola. He suggested that better healing would be obtained if red light were employed. During some unpublished experiments I carried out in collaboration with Captain S. R. Douglas, we were able to show that after the intravenous injection of neurovaccine into the ear-vein and blood-circulation of rabbits, the number of typical pustules which occurred from seven to ten days later over the skin of the abdomen and flank, was much less over an area of skin exposed to ultra-violet rays than on the normal non-irradiated skin. Further, the intensive ultra-violet irradiation of the rabbit's skin in no way aggravated the spread or healing of these lesions.

Apart from the exfoliative dermatitis and pustular ulcerative lesions which occur as direct result of exogenous or endogenous light-sensitization, confusion has arisen and statements have been made asserting that solar radiation aggravates many skin lesions. Infra-red and heat rays aggravate the irritation symptoms—i.e. itching discomfort—of many skin lesions; often these lesions flare up with any stimulus of heat. Erythema multiforme, acne rosacea and lupus erythematosis are such typical examples. The heat of bedclothes, or even the flushing of the face due to vasomotor and endocrine disturbances produces similar effects. It is possible that the erythema reaction following ultra-violet irradiation and the subsequent desquamation may originate a focus of irritation and the spread of a skin lesion due to some focus of infection or toxæmia. The pathological metabolic conditions may cause abnormal flora of bacteria or fungi in the large bowel which may contain some photo-sensitizing substance causing an abnormal skin reaction and aggravated skin lesion. Lupus erythematosis, acne rosacea, pityriasis streptogenes (Sabouraud), psoriasis, urticaria, and acute pemphigus have all been known to be markedly aggravated by exposure to sunlight.

Exogenous sensitization.—Skin lesions have been described amongst workers in coal-tar, creosote, and pitch, and following the use of flavine, eosin, and erythrosin. These are examples of the action of photo-dynamic substances absorbed by the skin cells.

Skin diseases following exogenous and endogenous sensitizers by common medicinal drugs and other chemotherapeutic agents.—The classical case of Meyer Betz (1913) is an example of exogenous sensitization due to hæmatoporphyrin. He received an intravenous injection of 0·2 grm. hæmatoporphyrin dissolved in 300 c.c. of saline (October 14, 1912) and remained light sensitive for several weeks, although tests of the blood and urine made on October 17, three days after injection of sensitizer, were all negative. The dose used, assuming he weighed 12 stone, was roughly 1 : 400,000 concentration for body-weight.

Endogenous sensitizers due to metabolism of the barbitone group. — The The barbitone group of drugs, trional, luminal, etc., themselves are not light-sensitizers, but cause products to be formed within the body which sensitize the visible rays.

Light dermatosis of agricultural domestic animals.—The skin lesions and light-sickness of domestic animals are mainly due to exogenous causes, due to the ingestion and absorption of chemical substances which are light sensitizers. Much of the present knowledge of photo-dynamic sensitization and the pathological reactions which follow solar radiation has mainly developed from the study of these skin lesions. Sensitization diseases of animals are only seen in white animals; they are uncommon in black animals; areas of pigmentation and coating with mud give protection. Feeding animals (sheep, pigs, cows, horses) with buckwheat causes erythema and œdema of the white areas of skin exposed to sunlight during the spring and summer months. The animals become very excitable and restless and death occurs from secondary infection of ulcerated areas of skin, causing cellulitis and general pyæmia. Tappeiner has shown that this is due to the presence of a fluorescent pigment which can be extracted from buckwheat plant or seed, and which is in every way a characteristic photo-sensitizer.

The photo-dynamic substance—according to Sheard and his co-workers—is phyloporphyrin. Hausmann states that buckwheat poisoning is unknown in man, owing to the destruction of the active principle by boiling. He states that the pigment hypericin phyloporphyrin is of interest owing to its close chemical relationship to hæmatoporphyrin.

Clover sickness is a condition seen in white horses, less seldom in cattle, fed on Swedish clover. The non-pigmented areas of the skin of the head, joints and mouth show reddening and œdema on exposure to bright sunlight. Necrosis of the skin and dropping off of the hooves may occur.

White sheep which have eaten hypericum crispum (crisp or cured hard hay), become very ill during bright sunny days; the woolly hair falls out and necrosis of the skin develops. Black sheep are immune. Joarrides has isolated a pigment from this hay which has proved to be a most potent light-sensitizer.

In Florida it is said that only black pigs are reared, as the white pigs become ill and die owing to the feeding with the pigment root of Lachnanth-Madder (Lachnanthes). The black pigs are immune.

The diseases of animals and man associated with abnormal reactions of the skin to light are therefore due to exogenous photo-biochemical substances, which sensitize the skin cells and deeper tissues to the luminous rays of the spectrum. Endogenous sensitization is comparatively rare. Inborn errors of metabolism and abnormal production of porphyrin pigments in the urine and fæces cause polymorphic, subacute, and chronic skin disease. There is some resemblance of these diseases to chronic types of radium and X-ray dermatitis. It is difficult to demonstrate the presence of photo-dynamic substances in the tissue fluids, owing to the very weak concentration present and to the lack of chemical, spectrographic, or biological means of analysis.

Future research should be directed towards the discovery of a therapeutic substance which will act as a sensitizer in the presence of blood-serum and be activated by the short infra-red, luminous, red, and orange rays.

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Section of Orthopædics

President—ALAN H. TODD, M.S.

[*December 5*, 1934]

Union of an Ununited Fracture of the Neck of the Femur following a Trochanteric Osteotomy.—S. A. S. MALKIN, F.R.C.S.Ed.

A. B., female, aged 56.

9.8.33: When first seen she said that eighteen months previously she had fallen and injured her right hip, had been treated in a plaster spica for six weeks, and had then commenced walking with a caliper splint. She complained of severe pain in the hip.

FIG. 1 (9.8.33).—Ununited fracture of the neck of the femur 18 months after accident. The line indicates the site of the subsequent osteotomy.

On examination.—There was grating on moving the right thigh. All movements were painful, and the leg was held externally rotated. The patient walked with a marked limp. A skiagram showed an ununited fracture of the neck of the femur.

14.9.33: A high trochanteric osteotomy was performed with the object of displacing the shaft of the femur inwards and buttressing up the line of fracture.

A plaster spica was applied and continued for six months. The patient walked in plaster two months after the operation.

6.4.34 : The osteotomy had united, and there was painless movement in the hip. The patient walked with the assistance of sticks.

FIG. 2 (12.11.34).—Showing firm union of the shaft with both the trochanter and the head of the femur and union of the fracture.

12.11.34 : The range of movement had increased to 30° of abduction and 60° of flexion. There was one inch of shortening and the patient had a slight limp, but she was free from pain and able to do her ordinary work.

A skiagram shows union of the osteotomy and of the fracture.

Fracture of Lower Fourth of Tibia and Fibula : Left Leg.—D. MCCRAE AITKEN, F.R.C.S.

I am indebted to the Orthopædic Department of St. Bartholomew's Hospital for the early history of this case. The boy was said to have broken his leg at the age of 9 months.

He was first seen at St. Bartholomew's Hospital in 1921, when about 2 years old, suffering from an ununited fracture of the lower fourth of the left tibia. Treatment with plasters and splints failed to secure bony union.

In 1924 the ends of the tibia were freshened, and a bone peg was tried. Non-union resulted. In 1925 a graft operation was attempted. In 1926 he was allowed up, with plaster and caliper. In 1927 he fell and fractured the fibula opposite the seat of non-union in the tibia.

When he was last seen at St. Bartholomew's Hospital in January 1928, the advice given was that the caliper was too short and should be lengthened.

In September 1928, six months later, when aged 9 years, he came under my care at St. Vincent's Orthopædic Hospital, Eastcote, with non-union of both bones, his caliper too short, and considerable deformity at the seat of fracture.

After four months of gradual correction in plaster, the limb appeared to be fairly straight. The tibia was exposed, the ends were freshened, and the limb was put up again in plaster. He was never allowed without a plaster for twelve months, until he was removed to the Fever Hospital, December 1929, with an attack of diphtheria.

He returned in February 1930, and again prolonged treatment in plaster was followed out, the patient being allowed to walk.

In December 1930, an attempt was made to graft the fibula, as there was a definite gap between its two ends. The ends of the tibia were only exposed, drilled and freshened. A prolonged period of continuous fixation in a succession of plasters, which were very carefully changed in order not to move the seat of fracture, resulted in union of the tibia eighteen months afterwards (May 1931). The boy was then allowed to walk without a caliper, but in plaster, and the bone consolidated.

In November 1932, he fractured the tibia at the same point when kicking a football. The fracture united without incident. The former graft of the fibula took at the lower end but not at the upper, so that there was now an overlapping of the two bones where there had formerly been a gap.

In 1934 the overlapping bones were freshened and tied together, and the latest skiagrams seem to show a slight degree of union of these overlapping bones. The tibia, however, has remained firmly united, and the boy is now able to walk with a high boot, the shortening being over 2 in.

Mr. AITKEN said that the great difficulty in these infantile fractures was in obtaining absolute fixation over a period of months. Infantile fractures healed very quickly, and if movement was allowed to take place in a fracture of the lower end of the tibia, where the bone was not encased in a sheath of muscle, the two ends of the bone were apt to heal up separately before union took place. Grafting, in his experience, had not been very satisfactory, but in the cases which he had seen, prolonged fixation, sometimes for a year or two, and, sometimes, as in this case, for many years, had almost invariably ended in union.

In changing the plasters care had been taken to remove half the plaster at a time, replace it with a fresh plaster, and when this was set, remove the other half, thus completing the fixation without moving the limb at the seat of fracture. This appeared to be a very important part of the technique if definite union was to be secured.

Diminutive Femora in Severe Abduction.—A. ROCYN JONES, F.R.C.S.

M. D., a boy, aged 4½. Both thighs noticed at birth to be much stunted and abducted. Was first seen at age of 3 months. A skiagram showed very short femora which were much abducted, and the heads and necks of which were unossified. The tibiæ appeared to be normal.

The boy was seen again recently (fig. 1) and it was found that he had been walking about for the last nine months. The gait was waddling; the knees were situated just below the anterior superior iliac spines, and the child was very dwarfed in consequence. A skiagram (fig. 2) shows some growth of the femora, but increased abduction due to weight bearing; on the left side there is a faintly ossified head of the femur in the acetabulum with an apparent interval (cartilaginous neck) between it and the shaft.

It is proposed to apply prolonged traction on the lower limbs until the femora assume a normal relationship to the rest of the body, and then provide the child with walking calipers.

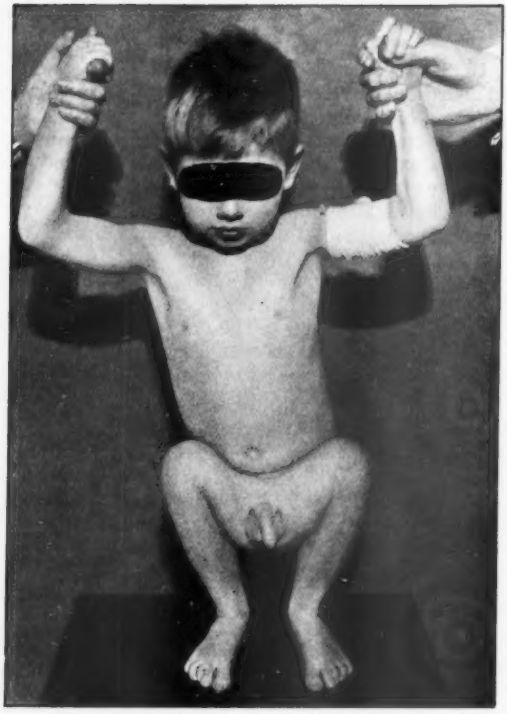

FIG. 1.—A boy, aged 4½ years, with diminutive femora which are so much abducted that the knees are at the level of the upper pelvis.

FIG. 2.—Showing the diminutive size of the femora. On the left-side there is a faintly ossified femoral head in the acetabulum.

Retarded Development of the Femur, with Coxa Vara.—A. ROCYN JONES. F.R.C.S.

J. P., a boy, aged 6. The right lower limb was noticed to be short at birth. Was first seen at the age of one month when the thigh was observed to be very short; the leg below the knee was normal. Abduction and internal rotation at the hip were limited but full flexion was possible. When the boy was aged 15 months (fig. 2) the limb was $3\frac{3}{4}$ in. short and a few months later he was provided with a walking appliance which consisted of a moulded leather thigh-piece to which was attached a walking patten. With this he walked quite well.

When aged 5 he was provided with an appliance resembling a bed caliper, except that the lower horizontal bar was replaced by a flat ring to make walking easier. The foot was enclosed in a leather gaiter to which were attached extension straps, and these were tied below to a bar just above the lower ring of the intrument. By this

FIG. 1.—J. P. (at age of $6\frac{1}{2}$ months), showing a very short femur with no apparent trace of a head or neck.

device, the child was enabled to get about freely, although the limb was completely relieved of weight-bearing. The foot was off the ground and moderate extension was continuously applied by means of the straps and gaiter. He still wears this appliance and by its means is enabled to attend school. He is now aged 6 years (fig. 3) and the limb is 6 in. short.

Three skiagrams are shown and it will be observed that at the age of $6\frac{1}{2}$ months (fig. 1) there was a very short right femur with no trace of a head and neck. Later, at the age of 15 months (fig. 2) an ossifying femoral head appeared, with an apparent gap between it and the shaft; but even at the age of five years there was no evidence of ossification of the cartilaginous neck. At the age of 6 years, however, ossification commenced in the neck.

It would appear, therefore, that in retarded development of the upper half of the femur it is to be expected that delay will occur in the ossification of the femoral

FIG. 2.—J. P., at the age of 15 months. An ossifying femoral head can be seen in the acetabulum and an apparent gap between it and the shaft (bridged by the cartilaginous neck).

FIG. 3.—J. P., aged 6 years. The femoral shaft has grown considerably; the head is well ossified and well formed; ossification of the neck is proceeding. There is a severe degree of coxa vara present.

head and that the neck will be delayed a few years longer before revealing itself in a skiagram by calcification. And, further, a severe degree of coxa vara appears to be the rule in these cases.

These skiagrams indicate that when such a case comes under observation in the first year of life the skiagram taken at that time may be misleading, in that only the shaft of the femur is revealed. It is safe, however, to assume that a cartilaginous head and neck are present but are subject to delayed ossification—particularly the neck.

Movements of the Lumbar Vertebræ during Flexion and Extension

By Philip Wiles, M.S.

At the meeting of the British Orthopædic Association at Cambridge in June 1933, Dr. A. E. Barclay showed some radiographs of the spine taken with the subject standing. The idea seemed such a good one, for the purpose of studying spinal movements, that since then, in conjunction with Dr. F. G. Nicholas, I have obtained a series of films taken by this technique at the Middlesex Hospital. I am greatly indebted to Dr. Nicholas and to the various "subjects" for their long-suffering coöperation.

Vertical radiography should prove of practical assistance in the routine examination of spinal deformities. The use of the method should provide no great

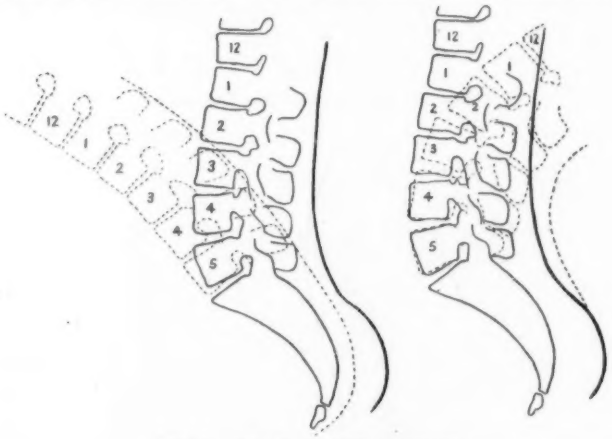

Fig. 1.—Miss P., aged 19. Masseuse.

difficulty, if the Potter-Bucky diaphragm is suspended by the apparatus devised by Mr. Norman Capener, who showed photographs of it, and of a number of films taken with it, at the last meeting of the British Orthopædic Association.

The purpose of the present investigation is to study the range and the nature of the movements of the lumbar spine during flexion and extension. Lateral radiographs were taken, using an ordinary plant, with the subject standing. Successive plates were exposed with an overlap of several vertebræ and a composite tracing made from these. The tracings of the upright and the flexed or extended positions were then superimposed, with the sacrum as the fixed point.

Four people are illustrated here. Two of them are massage students and may be regarded as normal active women (figs. 1 and 2). The other two are professional

acrobatic dancers: P.S.P. (fig. 3), still a child, has an abnormal range of flexion of the spine. Jig-Saw (fig. 4) is a man of colour and has abnormal powers of extension.

Tabulated on page 29 is the range of flexion and of extension of the lumbar spines of these four people, measured in degrees of deviation from the upright position.

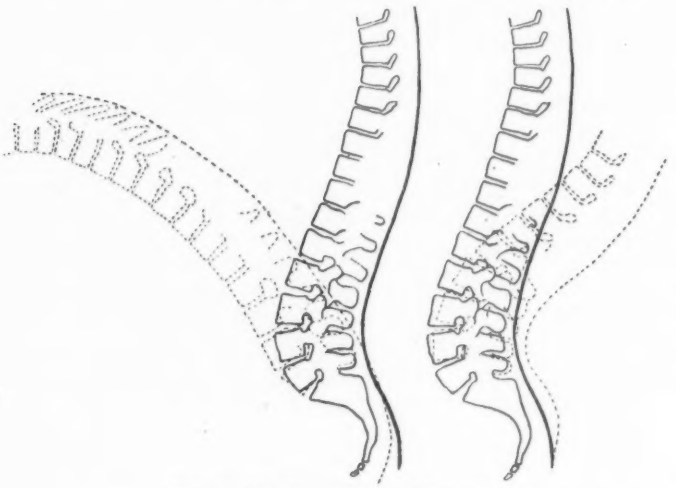

FIG. 2.—Miss R., aged 26. Masseuse.

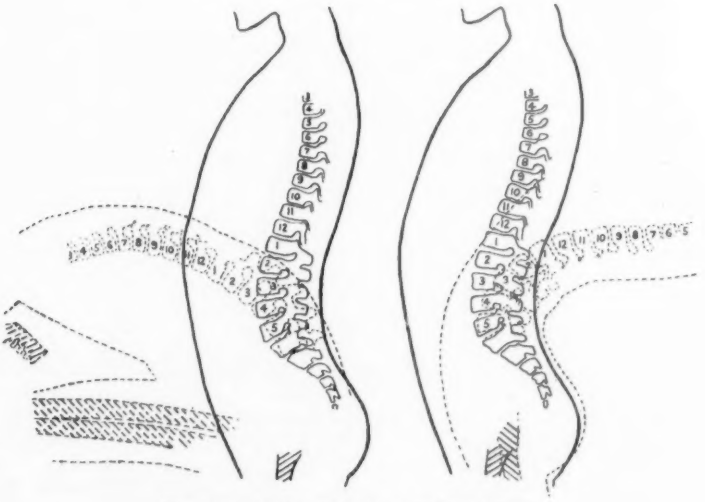

FIG. 3.—P. S. P., aged 12. Acrobatic dancer.

Measurements are made from the upper border of the sacrum to the lower border of the first lumbar vertebra, and therefore include five joints (Table I). The tracings also show the range of the lower dorsal spines of the two acrobatic dancers.

Measurements are from the top of the first lumbar vertebra to the bottom of the sixth dorsal vertebra, that is seven joints.

TABLE I.

	Degrees of flexion	Degrees of extension	Total movement	Average per joint
Lumbar spine				
Miss P.	64	35	99	20
Miss R.	62	19	81	16
P. S. P.	76	39	115	23
Jig-Saw	50	71	121	24
Lower dorsal spine				
P. S. P.	46	21	67	9·6
Jig-Saw	13	47	60	8·6

As with most acrobats, a great part of the movements occurs in the hip-joints. P. S. P. can do an honest "splits" of 180°, without any rotation of the pelvis at the hips. Jig-Saw has a truly remarkable dorsal spine in that he can literally hyperextend it (fig. 4). He has also at least 90° of rotation spread over the lumbar and dorsal spines.

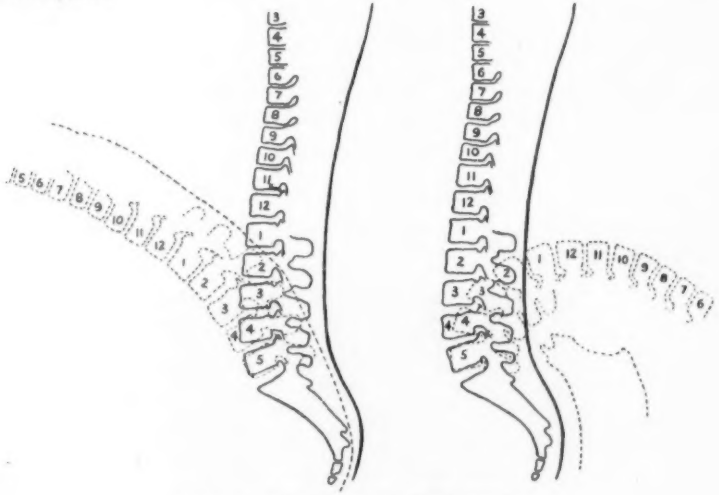

FIG. 4.—"Jig Saw." Acrobatic dancer.

The nature of the movements between a pair of vertebræ is complicated. It consists of rotation, lateral bending, flexion, and extension. The movements involved in lateral bending are essentially the same as those in flexion, and extension. Rotation is not considered here, except to point out that it must be reduced whilst in the extremes of the other positions.

The movements of flexion and extension occur in the joints between the articular processes and also by means of a change in shape of the intervertebral disks. The substance of the disks is such that an absolute change in their size is not to be expected. It is suggested that the change in shape occurs during flexion by compression of the disk in front and expansion behind; and during extension by an elongation and narrowing of the disk.

Table II expresses the height of the intervertebral disks in the upright position, flexion, and extension, as percentages of the height of the vertebral bodies. All measurements are made at the front of the bodies. It is interesting to notice that the two very flexible spines have thicker disks.

TABLE II

	Miss P.	Miss R.	P. S. P.	Jig-Saw
Flexed	17	21	21	29
Upright	32	35	45	42
Extended	38	41	55	64
Difference between flexed and extended ...	21	20	34	35

The articular processes are not, as might be expected, a fixed axis about which flexion and extension take place; instead, there is an up-and-down gliding in the articular joints. This was shown by drawing lines on the tracings to join the first

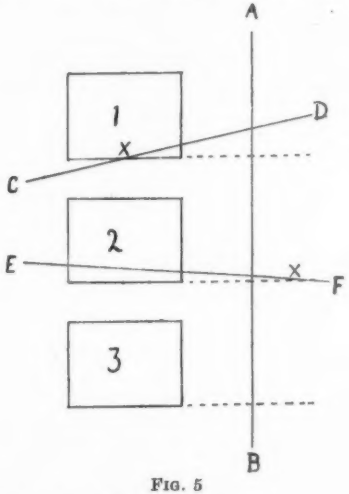

FIG. 5

A...B Plane of articular processes.
C...D Line of lower border of first lumbar, in flexion.
E...F Line of lower border of second lumbar, in extension.
X_1X... Axes of movement, at extremes of flexion and extension. In intermediate positions of the spine, the axis lies between these points.

lumbar vertebra and the upper border of the sacrum, in three different planes: the front of the bodies of the vertebræ, the articular processes, and the tips of the spines. If these distances are measured in the different positions of the spine, the axis of movement can be found. In Table III is given the percentage change in length of the lumbar spine in the plane of the articular processes during flexion and extension, as compared with the upright position.

TABLE III

	Miss P.	Miss R.	P. S. P.	Jig-Saw
Flexion ...	16	?	25	24
Extension ...	3	3	4	5

Somewhat surprisingly, these figures show that the line through the articular processes increases in length during both flexion and extension. The axis is there-

fore movable and does not lie in a fixed plane. In full extension of the spine it lies just behind the articular processes. As the spine is straightened, the axis moves forwards. In the upright position it lies approximately in the line of the articular processes, and in full flexion, near the median plane of the bodies. By combining the observations in Tables II and III, the movements can be shown diagrammatically (fig. 5).

Extension is limited by contact between the spinous processes. Flexion is limited probably by the interspinous ligaments and the joint capsules.

In addition to the movements already described, there is, during flexion, slight forward displacement of each vertebra on the one below it; and during extension a slight backward displacement. This is seen from the change in the alignment of the bodies, and the change in shape of the intervertebral foramina. The tracings of P.S.P. are exceptional, in that they show, during flexion, a backward displacement of the fifth lumbar and first sacral vertebræ, possibly on account of the lordosis when standing. It will also be interesting to see if this child has a permanent lumbarization of the first sacral vertebra.

This bodily displacement of the vertebræ produces a shearing strain on the intervertebral disks. It is likely to be of considerable importance in the production of the radial tears in the disks and injuries to the cartilage plates, described by Schmorl, and consequently in nuclear prolapse. Lambrinudi has recently drawn attention to the part played by short hamstrings in the ætiology of adolescent kyphosis. He considers that the forced flexion encouraged by gymnastic instructors may damage the disks if the hamstrings are short. It seems reasonable to suppose that such movements may produce a shearing strain on the disks greater than the limit of their tolerance.

Amniotic Band.—E. LAMING EVANS, C.B.E., F.R.C.S.

Baby H., aged 3 days. Right hand: Amniotic band embracing first finger and thumb at level of first interphalangeal joints (*see* photograph). The band has

12.10.34

produced: (1) A furrow in the fifth finger; (2) so-called intra-uterine amputations of the third and fourth fingers. The band now persists, binding together the index

finger and the thumb, and lying in furrows to which it is attached. Thus we have furrows, amputations, and a persistent band in one case. The left hand shows suppression of the middle and ring fingers. The left foot shows fusion of the first, second and third digits.

The child is otherwise healthy.

The following cases were also shown :—

Deformity of Wrist.—E. LAMING EVANS, C.B.E., F.R.C.S.

Osteochondritis of Spine.—S. A. S. MALKIN, F.R.C.S.

Osteochondritis of Spine.—D. MCCRAE AITKEN, F.R.C.S.Ed.

Cysts of Carpal Scaphoid.—H. JACKSON BURROWS, F.R.C.S.

Arthrokatadysis.—GWENDOLINE SMITH, F.R.C.S.

Myositis Ossificans.—B. WHITCHURCH HOWELL, F.R.C.S.